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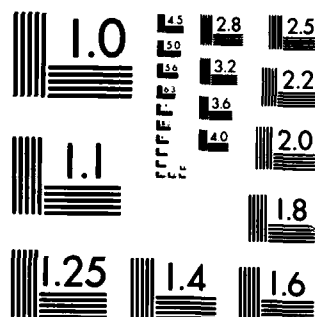
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SPRAY PYROLYSIS AS A SYNTHETIC TOOL

Final Technical Report

by

Dr. OTTO METH-COHN, Dr DALPAT PATEL, and

Dr. ROBERT K SMALLEY

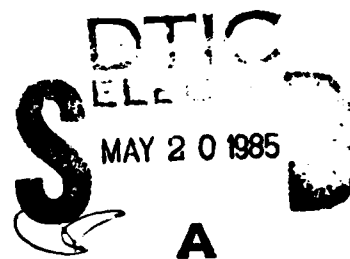
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The project is concerned mainly with the solution thermolysis and spray vacuum pyrolysis (SVP) of acyl and aryl azides. Under the latter conditions alkyl azidoformates (Ar(CH ₂) _n OCON ₃ ; n = 1 or 2) yield 5:7 or 6:7 fused 1H-azepines. The majority of the 5:7 fused systems are unstable and undergo rapid [6 + 4] dimerisation. In contrast, the 6:7 fused		

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systems are stable; the difference in stability is discussed in terms of the hybridisation of the bridgehead nitrogen.

Attempts to trap aryl nitrenes intramolecularly by suitably placed OH and NH₂ groups have failed. However, some novel polyheterocyclic structures have been obtained from the photo- and thermal decomposition of β -hydroxyethyl o-azido-benzoate.

The thermal decomposition of aryl azides in phenyl isocyanate yields 1-phenyl-3-phenylcarbamoyl-2-oxobenzimidazoles. In some cases N-arylcarbamates (p-XC₆H₄NHCO₂Me) are produced. The mechanism of this surprising reaction is discussed.

The behaviour of C-(o-azidobenzoyl) derivatives of alkyl ketones and esters on thermolysis and SVP is unpredictable and leads to a variety of heterocyclic products, dominant amongst which are 2,2-disubstituted indoxyls and 2,1-benzisoxazoles.

Anomalous behaviour is shown by o-azidobenzoyl malononitrile which on thermolysis yields a tetrazoloquinolone. The mechanisms of these reactions are discussed.

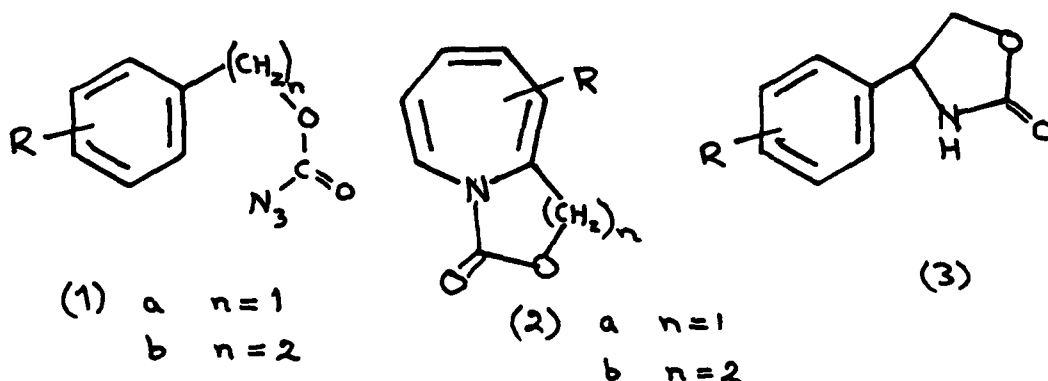
Pyrolysis studies on derivatives of 3-formyl-2,1-benzisoxazole, for which a new synthesis has been developed, show in contrast to the 3-(β -styryl)-2,1-benzisoxazoles, from which 3-aryl-1H-quinolin-4-ones are obtained, that 2-substituted indoxyls are the major products. Mechanistic aspects of these rearrangements are discussed.

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Summary

This project is concerned mainly with the solution thermolysis and spray vacuum pyrolysis (SVP) of acyl and aryl azides.

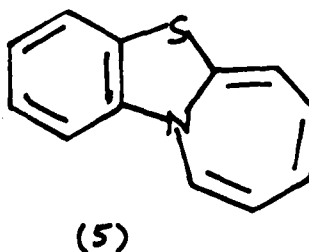
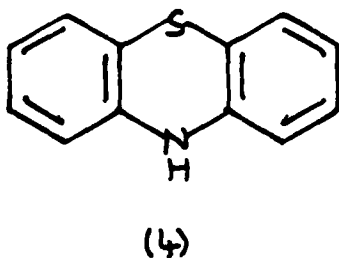
Under the latter conditions alkyl azidoformates (1) yield fused 1H-azepines (2a,b) of varying stability. The majority of the oxazolo-azepines (2a) are unstable and undergo rapid [6 + 4] dimerisation. In contrast, the oxazino-azepines (2b) are stable. This difference in reactivity is attributed to the pyramidal (or amine-like) character of the nitrogen in the systems (2a) and the sp^2 (or amide-like) nitrogen in systems (2b). Spectral and chemical data support this view.



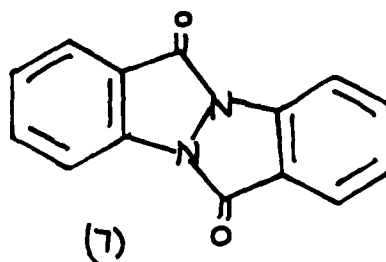
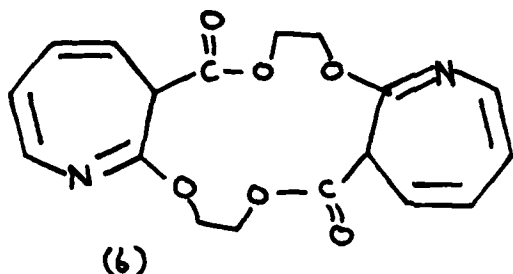
Some (4 + 2) cycloadditions of azepines (2b) are described.

Although acyl nitrenes show a marked tendency towards insertion into alkyl side chains, this alternative reaction to give oxazolidinones (3) is observed only in a few cases, and then in minor amounts.

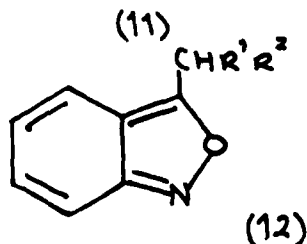
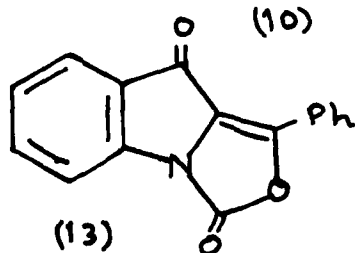
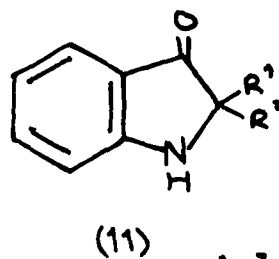
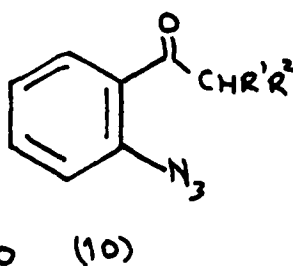
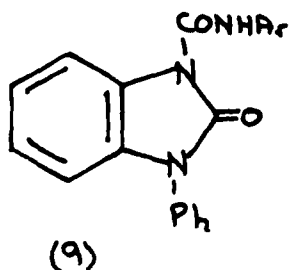
Azidoaryl phenyl sulphides on SVP, as on thermolysis in solution, yield phenothiazines (4) rather than the hoped for thienoazepines (5).



Attempts to trap aryl nitrenes intramolecularly by suitably placed OH and NH₂ groups have failed. However, some interesting polyheterocyclic structures (6) and (7) have been obtained from the photo- and thermal decomposition of β -hydroxyethyl *o*-azidobenzoate.



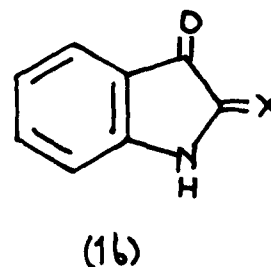
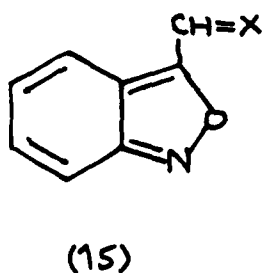
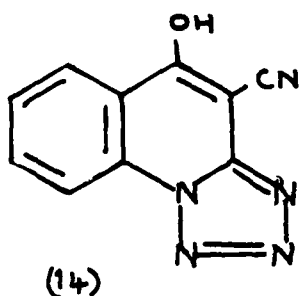
The thermal decompositions of aryl azides in phenyl isocyanate yield 1-phenyl-3-phenylcarbamoyl-2-oxobenzimidazoles (9). In some cases *N*-arylcabamates ($p\text{-XC}_6\text{H}_4\text{NHCO}_2\text{Me}$) are produced during work-up in methanol. The mechanism of this surprising reaction is discussed.



The behaviour of azidoacyl derivatives (10) on thermolysis and SVP is unpredictable and leads to a variety of heterocyclic products, dominant amongst which are indoxyls (11), and 2,1-benzisoxazoles (12). However, in two examples (10; $R^1 = \text{COPh}$, and COCH_3 , $R^2 = \text{CO}_2\text{Et}$) novel tricyclic products (13; $R = \text{Ph}$ and Me) are produced. The mechanisms of these cyclisations are discussed.

Anomalous behaviour is shown by the azidoacylmalononitrile

(10; $R^1 = R^2 = \text{CN}$); which on thermolysis yields the tetrazoloquinolone (14) via an intramolecular 1,3-dipolar cycloaddition.



Pyrolysis studies on 3-substituted-2,1-benzisoxazoles, in particular, those derived from 3-formyl-2,1-benzisoxazole, (15; $X = \text{O}$) for which a new synthesis has been developed, are reported. In contrast, to 3-(β -styryl)-2,1-benzisoxazoles (15; $X = \text{CHAr}$), which on thermolysis at 220°C yield 3-aryl 4-quinolones, these aldehyde derivatives yield mainly indoxyls of general structure (16). Mechanistic aspects of these rearrangements are discussed.

Keywords

Spray Vacuum Pyrolysis (SVP)

Thermolysis

Pyrolysis

Alkyl azidoformates

1H-azepines

[6 + 4] dimerisations

[4 + 2] cycloadditions

Aryl isocyanates

Aryl azides

2-oxobenzimidazoles

o-Azidoaryl ketones

Indoxyls

2,1-Benzisoxazoles

1,3-Dipolar Cycloadditions

Aryl nitrenes

Acyl nitrenes

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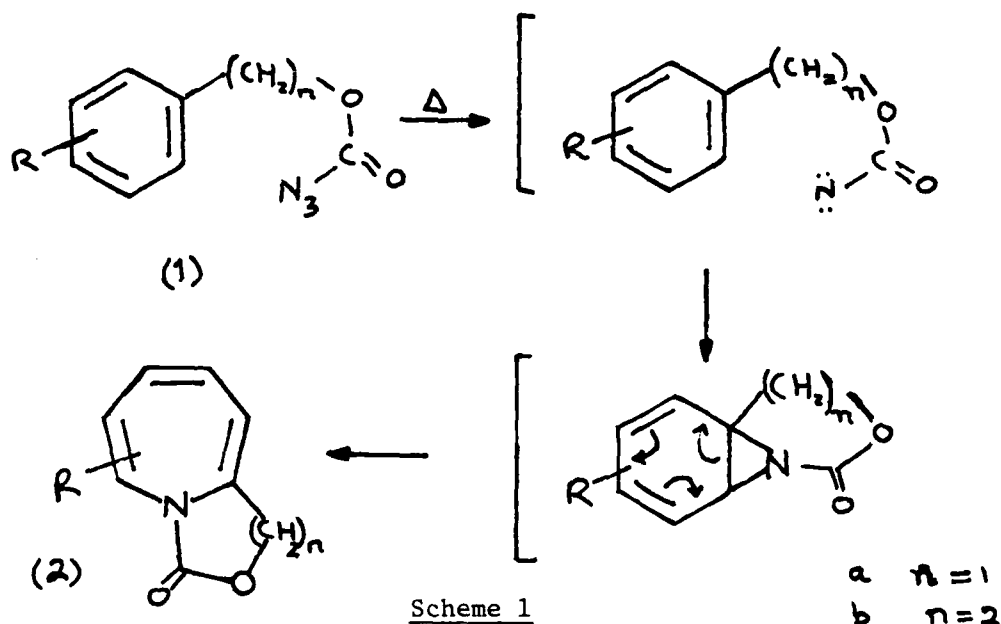
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O.Meth-Cohn and S. Rhouati, J. Chem. Soc., Chem. Commun.,
1980, 1161.
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Tetrahedron Lett., 1982, 23, 5085.
- Appendix C
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M. Clancy, D.G. Hawkins, M.M. Hesabi, O. Meth-Cohn, and
S. Rhouati, J. Chem. Res. (S), 1982, 78.
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p.54 Pre-print of a paper entitled '3H-Azepines and Related
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Some Acyclic Crown Ether Analogues'. by M. Azadi-Ardakani,
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Trans. 1, 1984, 2587.

Section 1

Spray Vacuum Pyrolysis of Alkyl Azidoformates. The Formation and Dimerisation of 1,2-Fused 1H-Azepines

One of the first objectives of this project, which was carried out under the direction of Dr. O. Meth-Cohn, was to synthesise and to investigate the chemistry of the 1,2-fused 1H-azepines (2a,b), prepared by spray vacuum pyrolysis (SVP) of benzyl and phenethyl azidoformates¹ (1a,b) as outlined in Scheme 1.

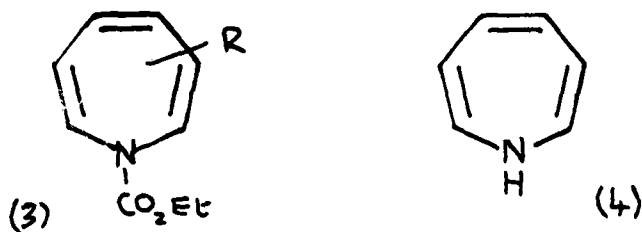


Intermolecular cycloaddition of the acyl nitrene to the arene nucleus followed by electrocyclic ring-opening of the tricyclic aziridine so-formed accounts for the formation of these novel heterocycles. The production of 1-acyl-1H-azepines by the analogous intermolecular addition of acyl nitrenes to arenes is well-documented.^{2a}

Of particular interest were the propensities of these systems towards (6 + 4) dimerisation, and their reactivity towards intermolecular (4 + 2) cycloadditions.

The background to the early stages of this work are described in the attached publications (Appendix A and B). Also attached (Appendix C) are details of the spray vacuum pyrolysis apparatus used throughout this project.

The most notable difference between azepines (2a) and (2b) was their ease of dimerisation. The oxazoloazepines (2a), as outlined in Appendixes A and B, readily dimerised, whereas the latter were stable crystalline monomers. A clue to the reason for this marked difference in stability was their colour. The only stable isolable oxazoloazepine was the dichloro-derivative (2a; R = 3,7-diCl) which proved to be bright-orange, as were all the transiently observed monomers of the dimers prepared and listed in the Table in Appendix A. In contrast, the oxazino-azepines (2b), like the well-known 1-acyl- (3) and 1-sulphonyl 1H-azepines^{2b} were invariably pale-yellow or white.



This visual evidence was further corroborated by examination of the absorption spectra of (2a) and (2b) in the ultraviolet and visible region (Table 1).

The highest wavelength absorption in the 6-fused azepine series (2b) was a broad envelope tailing into the visible region. This tailing was shifted to higher wavelength by 70 nm and λ_{max} by 42 nm in the comparable 5-membered analogue.

Clearly, these results indicated a considerable increase in conjugation in the azepines with a fused 5-membered ring compared to the higher or acyclic analogue. This must be due either to a greater

Table 1

Longest wavelength absorption of azepines (2a), (2b) and (3)

Azepine		λ_{\max} (nm)	E	approx. Tail absorption(λ)	Colour
No.	R				
(2b)	3,7-Cl ₂	358	516	470	Orange-red
(2b)	3,7-Cl ₂	316	1303	395	White
(2b)	5-t-Bu	320	1086	420	Yellow
(2b)	5-OMe	330	1151	435	Yellow
(2b)	H	335	740	430	Yellow
(3)	H	330	570	430	Orange-red ³
(3)	2-Me	302	1015		Pale Yellow ³
(3)	2,7-Me ₂	285	2110		White ³

azepine ring planarity or else a more planar amide moiety - or both of these factors. Dreiding models were problematical in that the nitrogen atom may be considered to be either planar and trigonal (i.e. sp^2) or pyramidal (sp^3) or in between. Using a planar nitrogen, the 5-fused azepine (2a) revealed an almost flat azepine ring whereas the 6-fused azepine (2b) was considerably boat-shaped. This could be the key difference. However, employing the tetrahedral nitrogen, the azepine ring was boat-shaped in both cases but flatter in the 5-fused example.

Paquette³ argued that the longest wavelength absorption in the ultra-violet spectrum was due to conjugation of the ring nitrogen with the π -system. If this is the case then:

(a) 1-H Azepine (4) should be orange-red. Recently^{2c} this parent azepine was prepared as an unstable orange-red oil. However, its UV spectrum was not recorded.

(b) The C=O π -orbital of azepine (2a) should be less coparallel with the N-lone pair than it is in azepines (2b) (this is indeed indicated in Dreiding models employing a pyramidal nitrogen).

(c) Substitution that further inhibits this coplanarity should result in a bathochromic shift and vice versa.

Further light was shed on the matter from a study of the ^1H n.m.r. spectra of the azepines, and some typical comparable examples of the 5- and 6-fused homologues (2a and 2b) and various non-fused standards are shown in Table 2. The chemical shift of the 5-fused series (2a)

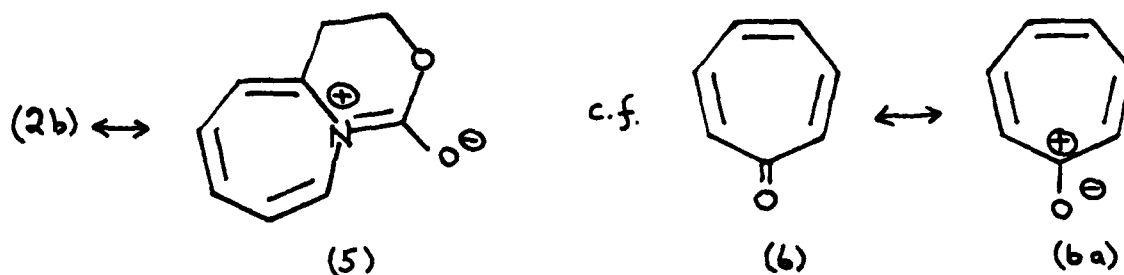
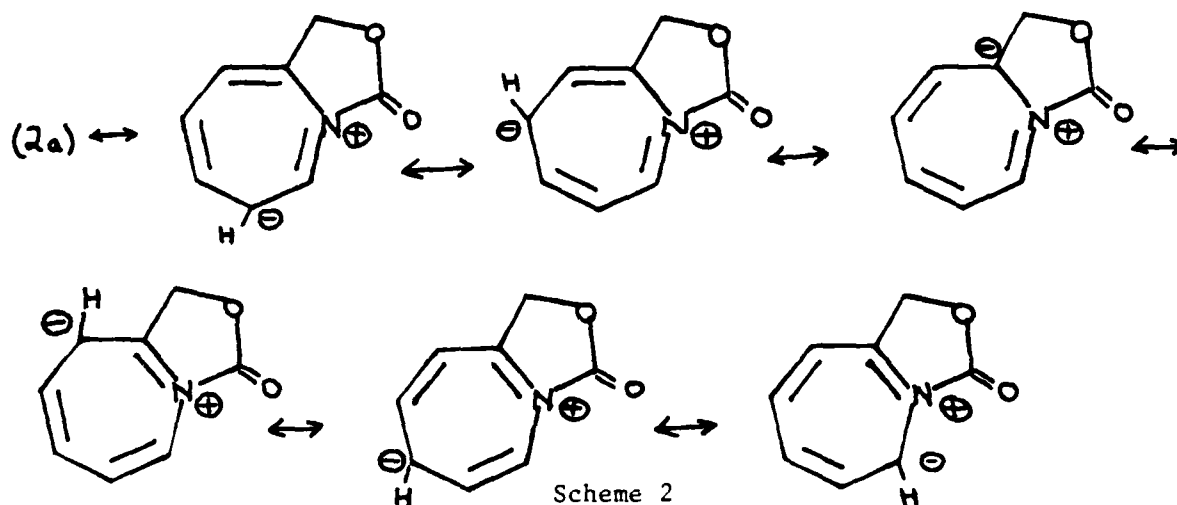
Table 2

^1H n.m.r. spectra of Azepines (2a), (2b), (3) and (4)

Compound		2	3	4	5	6	7	J (Hz)
No.	R							
(4)	-	5.22	4.69	5.57	5.57	4.69	5.22	$J_{23} = 7.9, J_{34} = 5.5,$ $J_{45} = 10.9$
(3)	H	5.82	5.42	6.10	6.10	5.42	5.82	
(3)	2-Me	-	5.62				6.27	
(2a)	5-Bu ^E	-	4.12	4.81	-	4.53	4.32	$J_{67} = 10, J_{34} = 8,$ $J_{2a3} = 2$
(2b)	5-Bu ^E	-	5.15	5.63	-	5.53	5.94	$J_{67} = 9, J_{34} = 6,$ $J_{2a2b} = 6$
(2a)	3,7-Cl ₂	-	-	5.5		5.9	-	
(2b)	3,7-Cl ₂	-	-	6.0		6.4	-	

were similar to those of 1H-azepine itself (4) while those of the 6-fused (2b) case were more like those of 1-alkoxycarbonylazepines.

A remarkable 0.5 to 1.0 ppm downfield shift of signals was noted for the 6-fused series compared to the 5-fused analogues, similar to that noted for comparison of azepine (4) with its methoxycarbonyl derivative (3; Me in place of Et). This data strongly supports the view that in the 5-fused series the nitrogen lone pair is conjugated with the π -system of the ring whereas the 6-fused azepines show amide resonance (5) and give a tropone ($6 \leftrightarrow 6a$) like mesomer (5) as illustrated in Schemes 2 and 3.



The latter system is clearly more akin to a 6π system while the former is an 8π molecule.

The ^{13}C n.m.r. data on comparable 5- and 6-fused azepines also corroborated our findings (Table 3) in that upfield shifts of the enaminic carbons of (2a) (carbons 3 and 6) were clearly evident (7.5 and 4.0 ppm respectively) in comparison with (2b). Furthermore the chemical shifts

Table 3

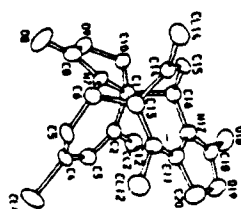
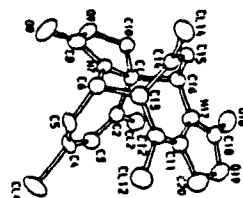
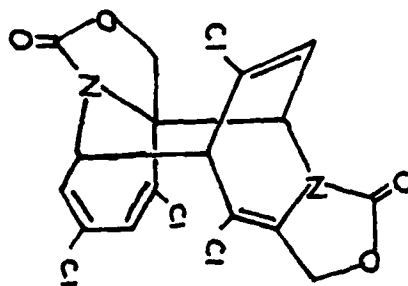
The ^{13}C n.m.r. of some 1H-azepines (2-4)- chemical shifts (ppm)

Compound		2	3	4	5	6	7	CO	Others
No.	R								
(4)	-	138.0	113.0	132.3	132.3	113.0	138.0	-	(Ref.4)
(3)	-	130.1	118.8	130.1	130.1	118.8	130.1	152.7	61.4 (CH_2), 13.9 (Me)
(2a)	5-Bu ^t	139.0	101.7	119.9	147.5	113.6	127.2	154.5	66.6 (2a), 35.4 (CMe_3), 27.7 (Me)
(2b)	5-Bu ^t	138.5	113.0	121.5	150.7	119.0	129.0	149.6	28.5 (2a), 66.7 (2b), 28.9 (Me), 35.3 (CMe_3)
(2a)	3,7-Cl ₂	139.8	114.2	127.1	131.3	119.3	122.8	152.2	69.1 (2b)
(2b)	3,7-Cl ₂	135.2	121.7	127.9	131.1	123.3	135.2	147.6	27.8 (2a), 66.4 (2b)

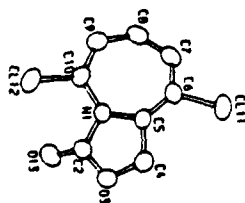
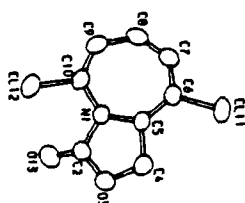
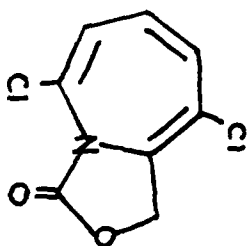
of oxazoloazepines (2a) were much closer to those of the parent azepine than were those of the 6-fused analogue.

X-ray crystallographic data on azepine (2a; R = 3,7-diCl) fully supported our opinions, in that the nitrogen appeared to be pyramidal and the azepine ring boat-shaped (see Figure).

In conclusion, it would appear that the oxazoloazepines (2a) are far from being planar 7-membered 8π antiaromatic ring-systems. However, the key feature that explains the dramatic differences in physical properties and chemical reactivities between these and their oxazino-analogues (2b) is the amine-like nitrogen in the former and the amide-like nitrogen in the latter.



ORTEP stereo view of an oxazolidinazepine and a related dimer.



Section 2

The Formation and Cycloadditions of Oxazino[3,4-a]-1H-azepin-2-ones

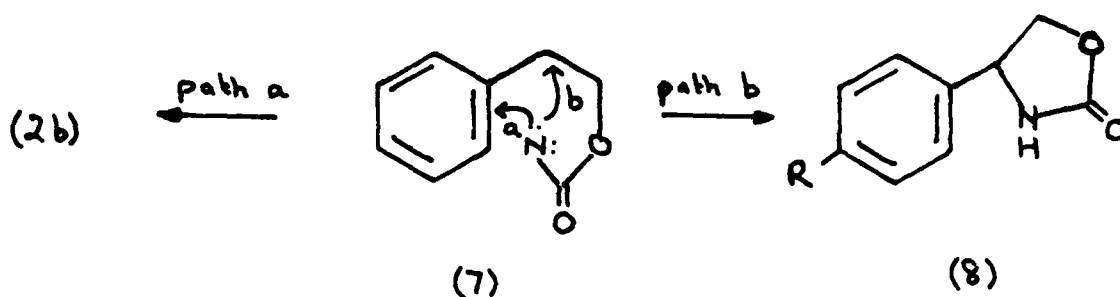
a) Azepine vs. Oxazolidinone Formation

A series of stable, monomeric oxazinoazepines (2b) were prepared (Table 4) in order to study their cycloaddition reactions. A persistent by-product in those reactions were the oxazolidinones (8), formed by a competing insertion reaction of the acyl nitrene (7) at the conveniently situated 2-methylene of the alkyl side chain (Scheme 4). The best yields of azepine were observed with electron-donating substituents R. Significantly the ratio of ring attack to side-chain attack diminished in order of nucleophilicity of the aromatic ring.

Table 4

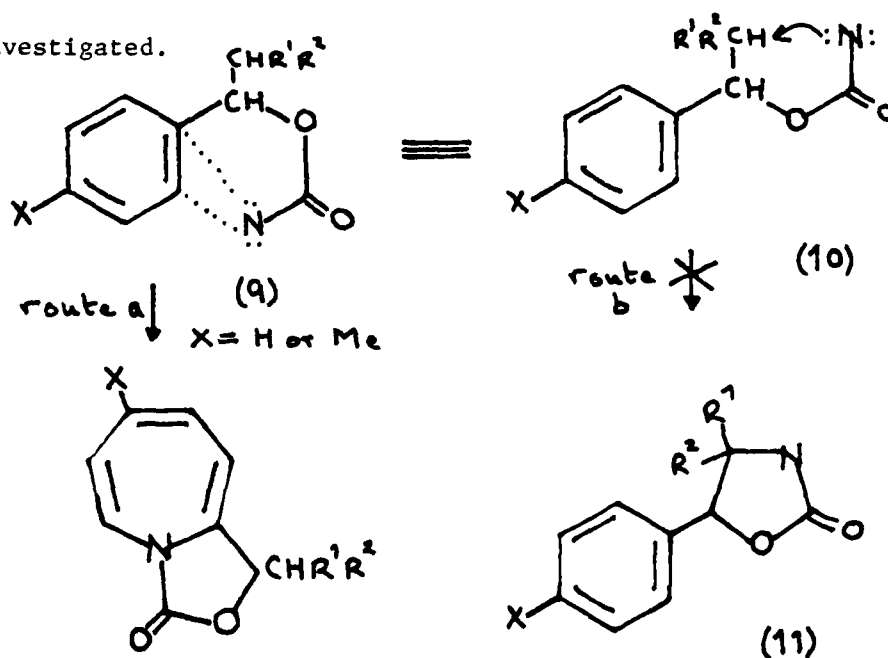
Oxazinoazepines (2b) and oxazolidinones (8) by Pyrolysis of β -Phenethyl azidoformates (1b)

Substituent R	% Yields		Ratio 2b/8
	(2b)	(8)	
MeO	61	10	6.1
Bu ^t	56	12	4.7
Me	54	29	1.9
Cl	38	22	1.7
Br	20	18	1.1
CN	0	trace	—
NO ₂	0	0	—



Scheme 4

The preference for acyl nitrenes to insert into CH bonds in the order tertiary CH > secondary CH > primary CH,⁴ suggested that the presence of an alkyl substituent at the benzylic carbon centre of benzyl azidoformates (1a) would promote oxazolidinone formation along with or in preference to, ring-expansion to oxazoloazepines. Accordingly, several α -substituted benzyl azidoformates (9a-d) have been prepared¹, and the selectivities of the acyl nitrenes (10a-d) generated under spray pyrolysis conditions, for insertion into the α -methine group (route b) against azepine formation (route a: Scheme 5) investigated.



(a) $R^1 = \text{Me}$, $R^2 = \text{H}$; (b) $R^1 = p\text{-MeC}_6\text{H}_4$, $R^2 = \text{H}$; (c) $R^1 = R^2 = \text{Me}$; (d) $\text{CHR}^1\text{R}^2 = t\text{-Bu}$

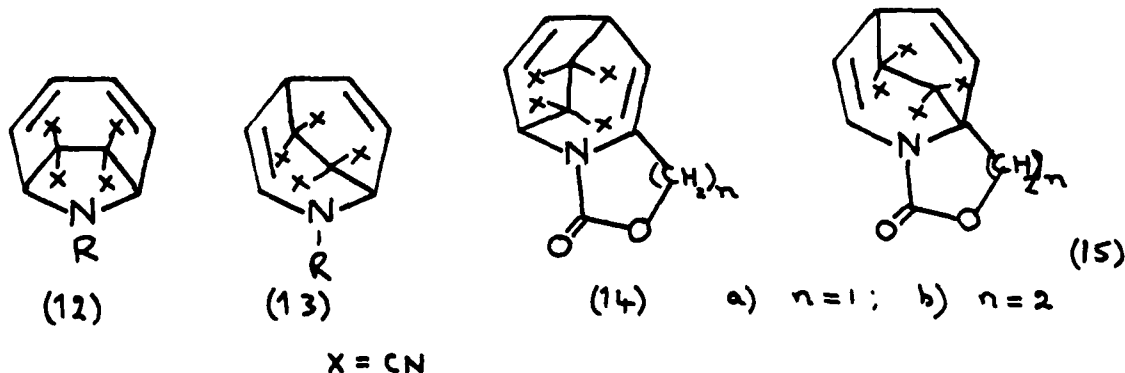
Surprisingly, however, in all the systems studied, azepine formation prevails regardless of the nature of the substituents R^1 and R^2 and no oxazolidinones (11) have been isolated.

The ethyl (9a) and *p*-methylbenzyl (9b) derivatives gave the syn azepine dimers analogous to those reported previously. (See Appendixes A and B). The isopropyl derivative (9c) behaved similarly but gave a mixture of the syn (22%) and anti (27%) dimers. Dimer production was also noted from the pyrolysis of the *t*-butyl derivative (9d).

Attempts to produce an oxazolidinone by a thermally-induced retro-dimer \rightarrow monomer \rightarrow aziridine \rightarrow aryl nitrene route was also unsuccessful. On heating in boiling bromobenzene, the syn-isopropyl dimer did in fact yield the monomeric azepine (detected by t.l.c.) but on cooling the reaction only a mixture of syn- and anti-dimers were obtained.

b) Cycloaddition Reactions with Fused Azepines (2a) and (2b)

Of the few effective cycloadditions accomplished with azepines those with tetracyanoethylene (TCNE) have been the most effective. Initial indications suggested a $[6 + 2]$ interaction to give adducts (12). However, several groups demonstrated the error of this

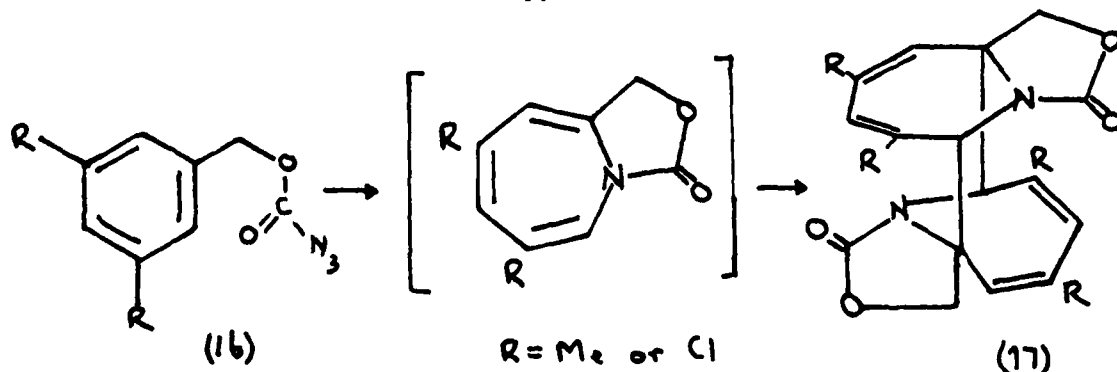


interpretation and proved that $[4 + 2]$ addition (13) had in fact occurred^{2d}. Site selectivity was observed with unsymmetrically

substituted azepines, a non-bridgehead substituted adduct always being preferred. Photis⁵ upset this orderly picture by noting that some 3,6-disubstituted azepines underwent $[6 + 2]$ cycloaddition in the cold; these adducts rearranging to $[4 + 2]$ adducts on heating. These results prompted a study of similar cycloadditions to the fused azepines (2a and 2b). All the adducts were formed rapidly in the cold and in every case $[4 + 2]$ addition occurred. However, in the 5-fused series (2a), while the 5-*t*-butyl and 3,5,7-trimethyl derivatives gave the adduct (14a), the 3,4,6,7-tetramethyl derivative gave the isomeric lesser substituted (15a).

In the 6-fused azepine series (2b) cycloaddition to all the substituted derivatives gave the (14b) mode of addition, i.e. the less substituted isomer only was formed. However, with the parent compound (2b; R = H) the isomeric (15b) mode of addition was noted. Attempts to rearrange thermally this more substituted adduct gave only a complex mixture of inseparable products.

The dimerisation of the azepines (2a) were shown (Appendix A) in all the cases studied, to give $[6 + 4]$ dimers as exo adducts in either the syn or anti form. In view of the results of Photis, which indicated $[6 + 2]$ adducts of 1H-azepines with TCNE, we further studied the pyrolysis of the 3,5-di-substituted benzylazidoformates (16) and were gratified to note that only $[6 + 6]$ dimers (17) were formed. No tendency towards further rearrangement of these adducts to $[6 + 4]$ dimers was noted. (See also Appendix A).



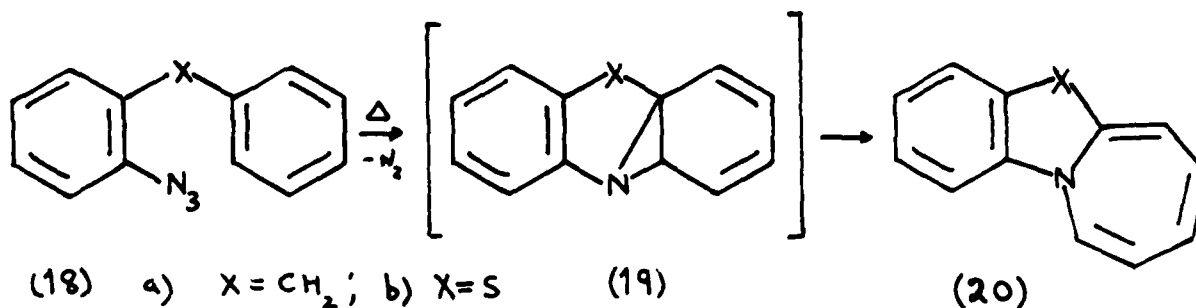
Section 3

Intramolecular Aryl Azide Reactions

a) Phenothiazine vs. Thienoazepine Formation during the Thermolysis of o-Azidophenyl aryl sulphides

The thermal decomposition of o-substituted aryl azides can lead to an interesting and varied array of heterocyclic products.⁶

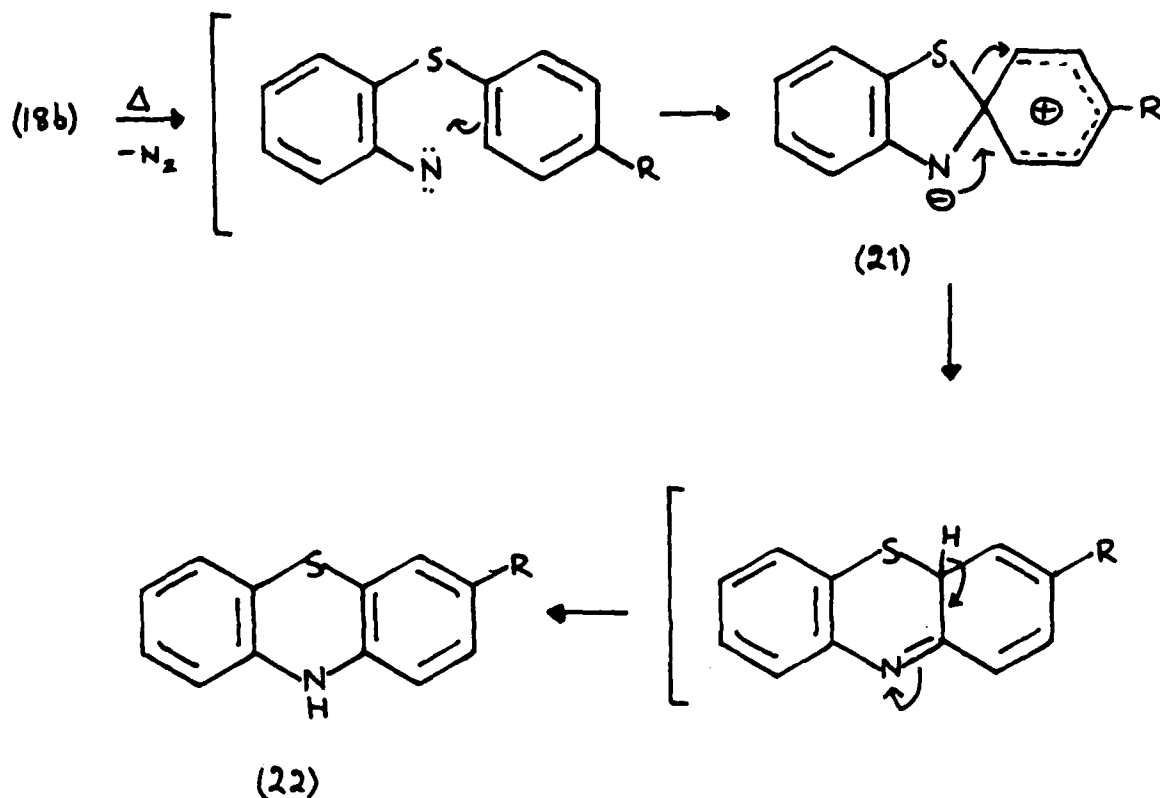
Of particular interest are those azides in which intermolecular cyclisation of the derived nitrene takes place at a suitably positioned aryl ring. For example, the 10H-azepinoindole (20a) was isolated⁷ from the decomposition of 2-azidodiphenyl methane (18a). Ring-expansion was thought to occur via ring-opening of the aziridine in the initially formed tetracyclic intermediate (19) as outlined in Scheme 6.



Scheme 6

In contrast, the corresponding azidosulphides (18b) gave phenothiazines (22),¹⁰ rather than thienoazepines, by a route involving the charged spirodienyl intermediate (21) formed by attack of the nitrene at the carbon centre bearing the sulphur substituent, (Scheme 7).

Migration of the sulphur function followed by a hydrogen shift provides the phenothiazine (22) in which substituent R has apparently undergone a shift from a position para, to one meta,



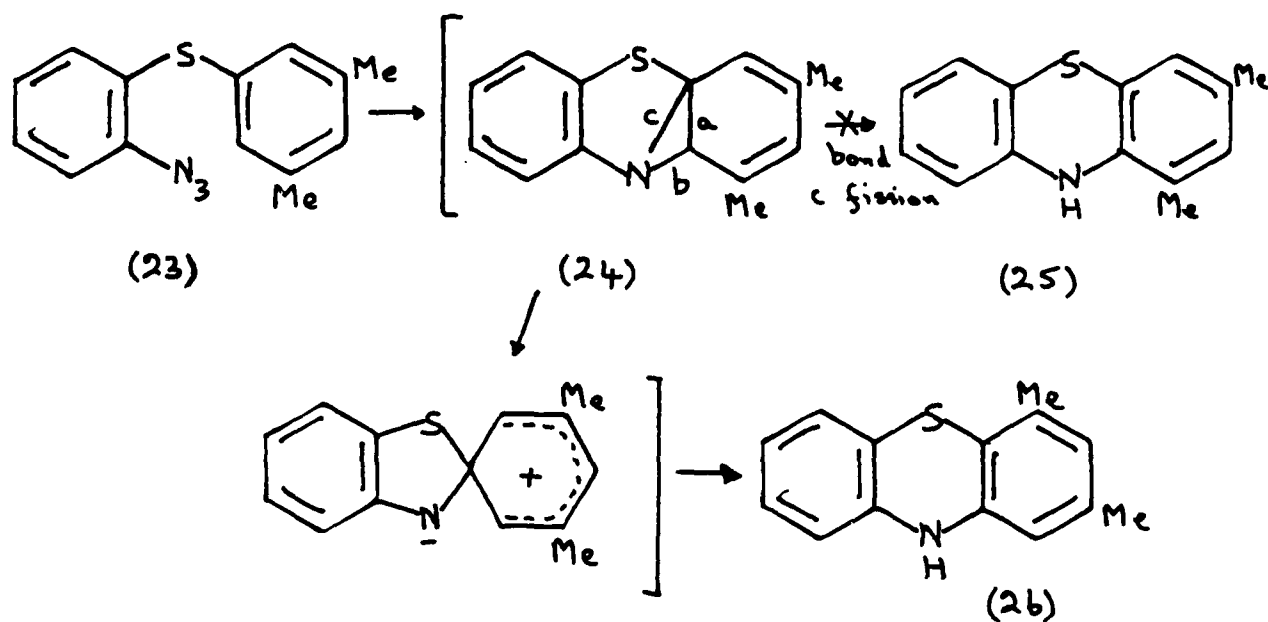
Scheme 7

to the sulphur atom. Many such rearrangements involving spirodiene intermediates are now known.^{8,9}

However, it is possible that a fused aziridine intermediate of type (24) is first formed in all cases, which by selective bond cleavage (Scheme 8) can give azepines (bond a fission), spirodienes (bond b fission) or phenothiazine (bond c fission) directly.

The spray pyrolysis of some substituted azido aryl sulphides was undertaken in an attempt to isolate thienoazepines, or unrearranged phenothiazines, indicative of such a common intermediate.

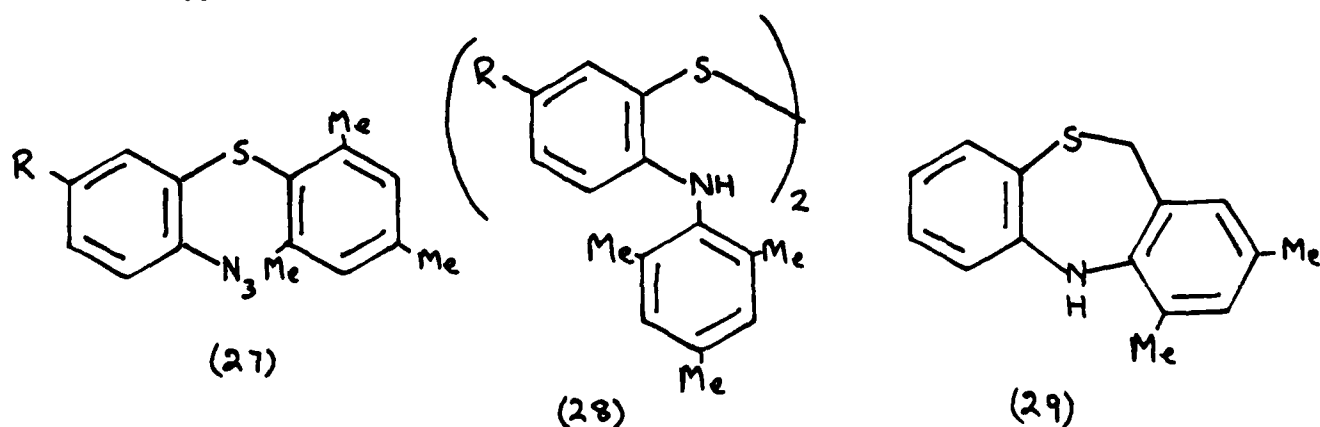
The azidodimethyldiarylsulphide (23) on pyrolysis gave a single product which from ¹H n.m.r. analysis was shown to be a phenothiazine rather than a thienoazepine. The product was, in fact, the rearranged 1,3-dimethyl derivative (26), and not the 2,4-dimethyl isomer (25) as would have been the case had route (c) been operating (Scheme 8).



Scheme 8

Identity of phenothiazine (26) was established by spectral data and by comparison with a known sample.¹⁰

Pyrolysis of the mesityl derivatives (27; R=H or Cl) were equally disappointing in that they gave the same products as those observed previously by Cadogan and his co-workers⁸ from the photolysis of these azides, namely the disulphides (28) and the dibenzothiazepines (29). No phenothiazines or thienozepines arising from an intermediate of type (24) were detected.



No evidence has been accrued to implicate the tricyclic aziridine (24) as an intermediate in the cyclisation of these

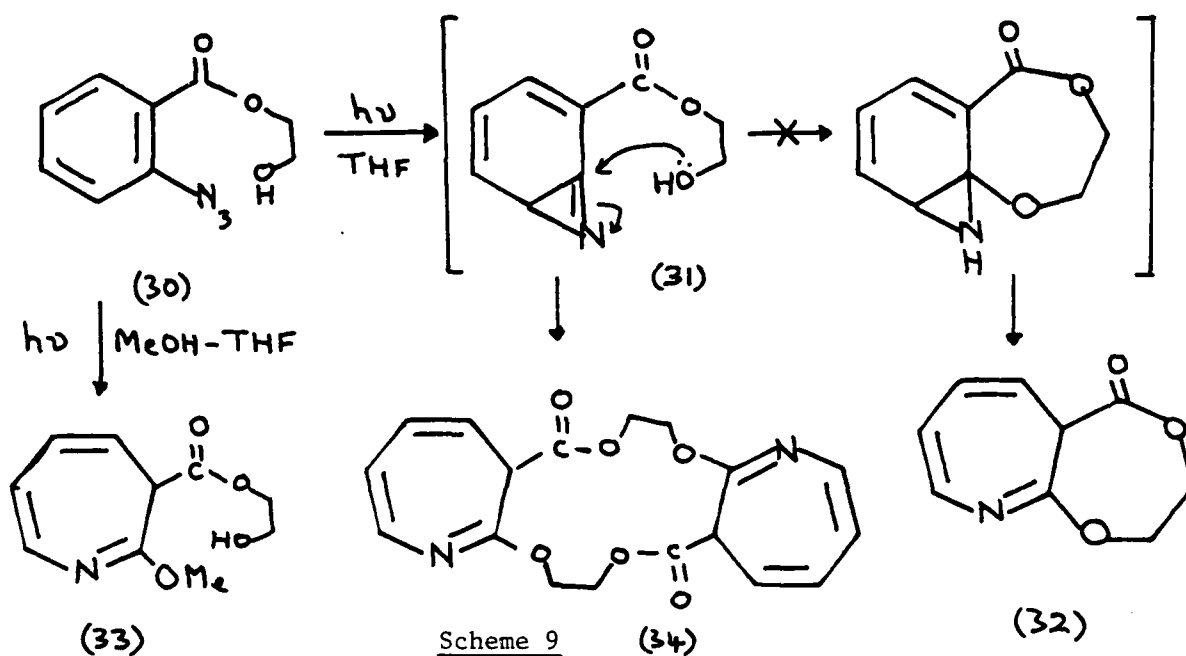
b) Intramolecular Trapping of Aryl Nitrenes

Thermolysis or photolysis of aryl azides under a variety of conditions produces mainly azo-compounds and arylamines as a result of triplet nitrene mediated reactions.⁶ However, in the presence of nucleophiles, notably amines and alcohols, ring-expansion to 2-amino- and 2-alkoxy-3H-azepines is observed.^{2e} Trapping of the singlet nitrene-benzazirine/or -azacycloheptatetrene^{11,12} intermediate by an alcohol is most efficient in those systems in which the azide has an ortho electron-withdrawing substituent, particularly an ester or amide.¹³ So far as we are aware, intramolecular trapping of this intermediate by a pendant nucleophilic side-chain has not yet been achieved. Therefore, it was of interest to pyrolyse azides of type (30) in which intra-molecular trapping of the intermediate (31: here shown as a benzazirine) would result in fused azepines of type (32) as shown in Scheme 9.

Pyrolysis of β -hydroxyethyl o-azides benzoate (30) in solution, in keeping with other simple alkyl esters, gave only tarry materials and traces of o-amino-ester. In contrast, photolysis of the azido-ester in a mixture of methanol and tetrahydrofuran produced the 3H-azepine (33) in practicable yield (56%). Interestingly, when the photolysis was carried out in tetrahydrofuran in the absence of methanol, the crown-ether like bis-azepine (34) was obtained, albeit in low yield (7%), rather than the hoped for intramolecularly produced, fused azepine (32).

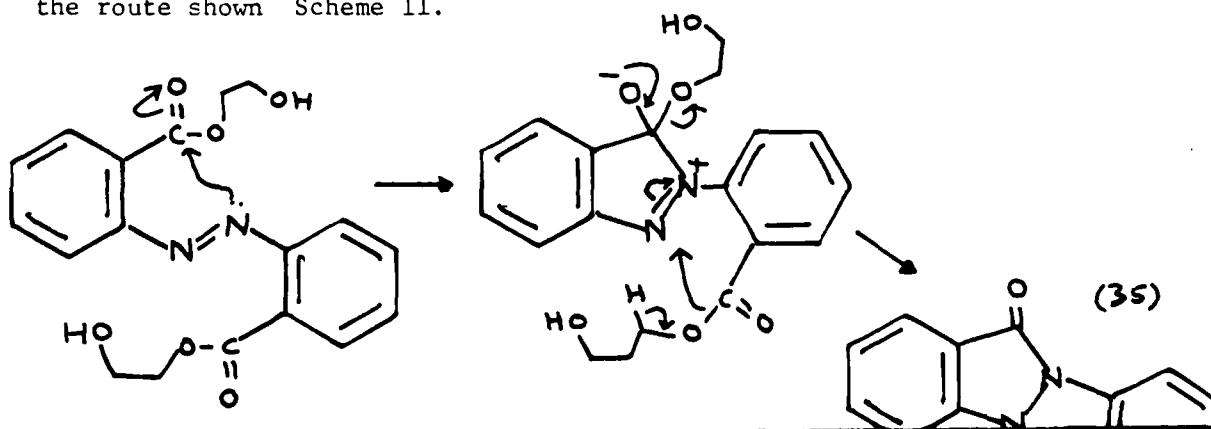
Formation of macrocycle (34) is surprising, and presumably arises by intramolecular nucleophilic additions of the glycol side chain to the benzazirine intermediate (31) as outlined in Scheme 2 in the Appendix D.

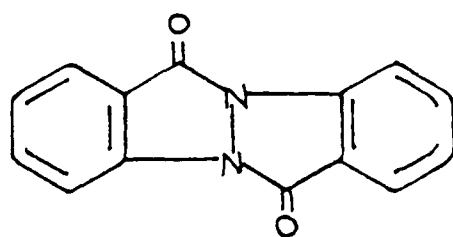
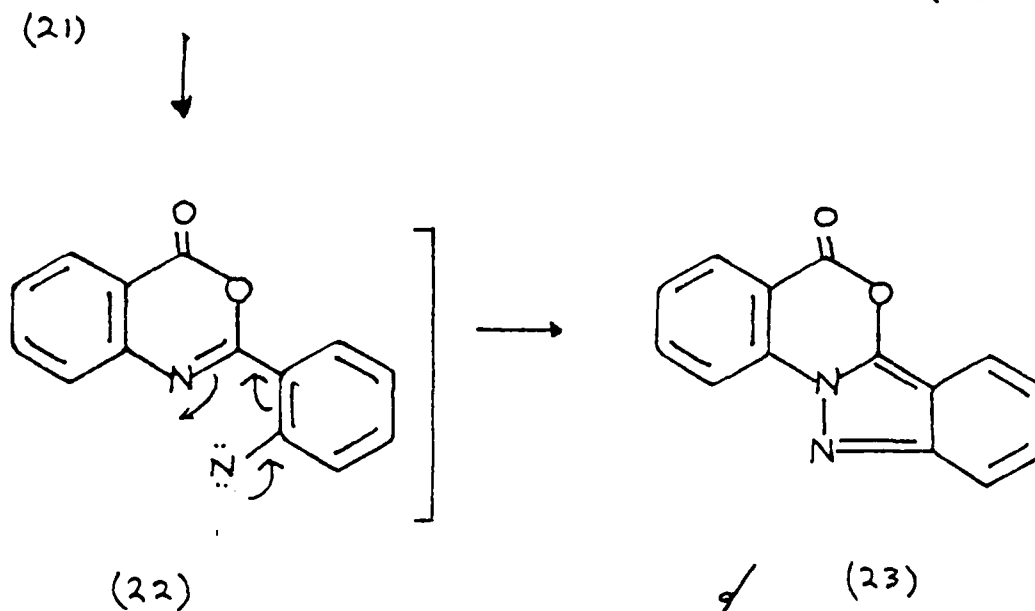
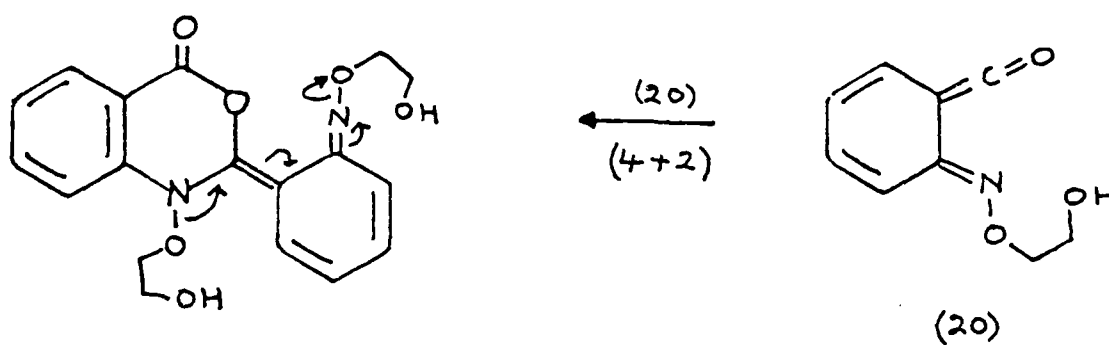
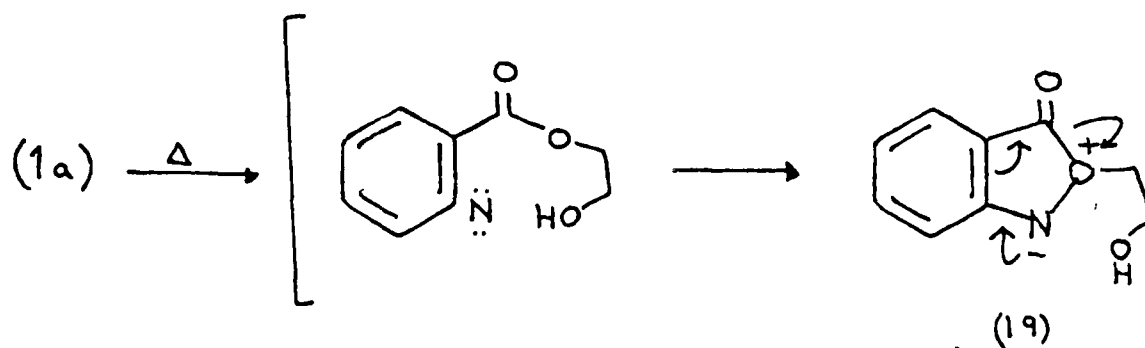
On subjecting the glycol ester (30) to SVP an equally unexpected

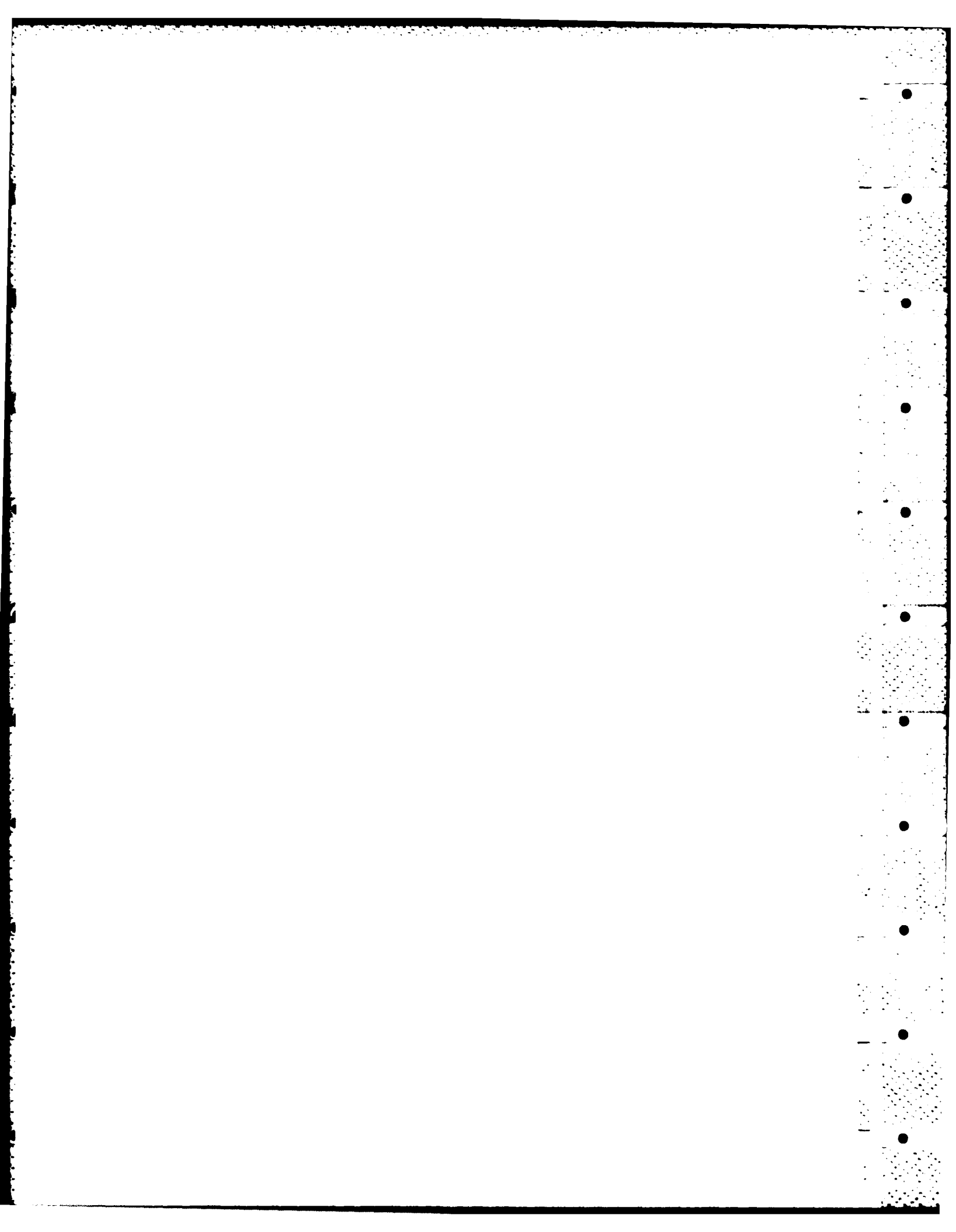


and surprising result was obtained in that the sole identifiable product, besides much tar, was the high-melting indazolo-indazolinone (35).

Coincidentally, we have recently been involved¹⁴ in the synthesis and reactions of this little known system. However, its mode of formation in this pyrolysis reaction is not yet clear. Originally,¹⁵ a complex but precedented reaction sequence was proposed (Scheme 10) the mechanism for which is discussed in Appendix D (page 8). Alternatively, the indazolo-indazolinone may have arisen by initial formation, during pyrolysis, of the azo-compound (36) (a typical triplet nitrene mediated by-product⁶), which on further pyrolysis cyclises by the route shown Scheme 11.

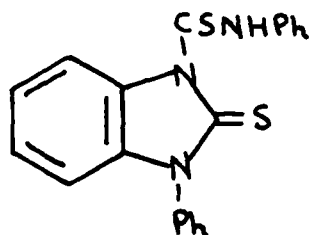
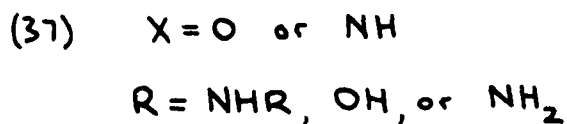
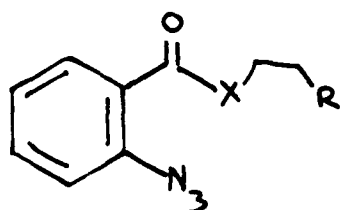




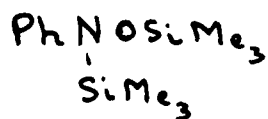


This reaction sequence is attractive on account of its simplicity, relative to Scheme 10, and also for the fact that the formation of tetracycle (35) during the photolysis of azobenzene-2,2'-dicarboxylic acid has been reported.¹⁶ So far however, we have been unable to obtain corroborative evidence for this reaction pathway. SVP of the preformed methyl or ethyl ester analogues of azo-compound (36) gave none of the indazoloindazolinone.

Other attempts to effect intramolecular trapping of the intermediate (31) using other azido-esters or -amides bearing nucleophilic side-chains e.g. (37) were unsuccessful. On SVP or on thermolysis in solution, only tarry uncharacterised products were obtained, along with, in some cases, the corresponding amino-esters.



(38)



(39)

Section 4

Thermolysis of Aryl Azides in Phenyl Isocyanate

This portion of the work which formed the bulk of the 4th Semi-annual Report, is about to be published in the Journal of the Chemical Society, Perkin Transactions I.¹⁷ This section is, therefore, described fully in a copy of this paper which is attached to this report as Appendix E.

Variations in the reaction conditions described in this paper produced disappointing results. Decomposition of phenyl azide or p-methoxyphenyl azide in a 10% solution of PhNCO in xylene, furnished in addition to much tar, only the N,N'-diarylurea. Presumably, the nitrene, as the triplet form, abstracts hydrogen from the solvent to give arylamine (a well-known process),⁶ which with isocyanate yields the urea.

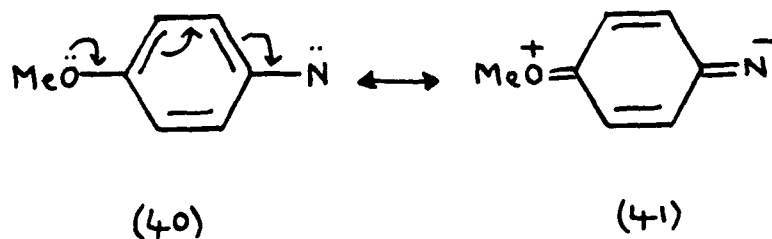
Photolysis of phenyl azide in phenyl isocyanate gave only azo-compounds. Similarly, when a mixture of phenyl azide and phenyl isocyanate were subjected to spray pyrolysis under a variety of temperatures and column packings, azobenzene was the sole identifiable product.

Decomposition of phenyl azide in phenyl isothiocyanate was messy but yielded, after careful chromatographic separation, a small amount of the benzimidazole-2-thione (38) (0.5%) and azobenzene (15.6%).

Attempts to generate benzimidazolinones by the action of aryl nitrenes derived from non-azide sources, on phenyl isocyanate have been disappointing. Deoxygenation of nitrobenzene with trimethyl phosphite⁸ in the presence of phenyl isocyanate gave only intractable tars. A more amenable approach appeared to be the thermal decomposition of N,O-bis-trimethylsilylhydroxylamine (39), which recently has been shown¹⁸ to be an excellent source of phenyl nitrene at relatively low

(100°C) temperatures. However, experiments involving the decomposition of the silyl derivative in boiling PhNCO yielded only small amounts (ca. 1%) of benzimidazolidone along with azobenzene (25%) and an uncharacterised, high melting product (34%).

The production of azo-compounds during these thermal and photochemical decompositions was not unexpected and probably involves dimerisation of a triplet aryl nitrene.^{6,19} Significantly, the yield of azo-compound during thermolysis of the aryl azides in phenyl isocyanate is greatest (see Table in Appendix E) with the least electrophilic nitrene (i.e. $p\text{-MeOC}_6\text{H}_4\text{N}$), and probably reflects the resonance stabilisation of the singlet nitrene ($40 \leftrightarrow 41$) which not only decreases its electrophilicity, but which also allows time for 'cross-over' to the triplet form, and hence azo-compound formation, to take place.

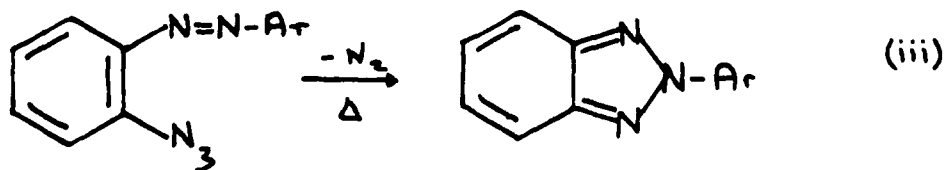
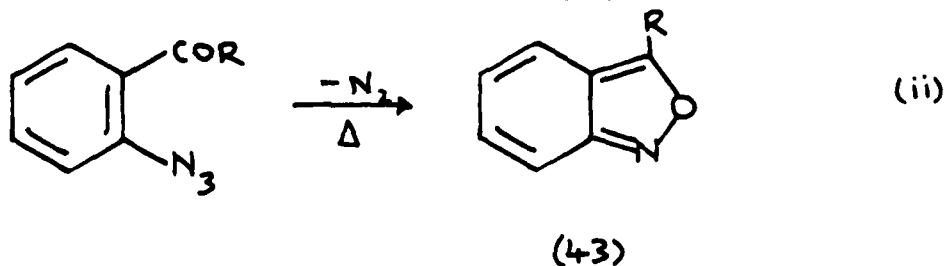
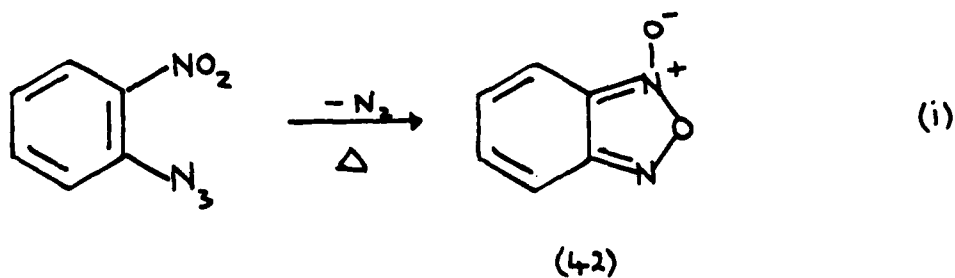


Section 5

Thermolysis and Spray Vacuum Pyrolysis of 3-Substituted 2,1-benzisoxazoles and o-Azidoaryl ketones

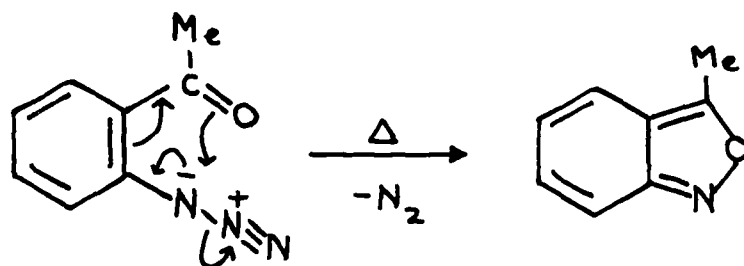
In general, the thermal decomposition of aryl azides proceeds via loss of nitrogen to yield an aryl nitrene, initially in the singlet (PhN), or electrophilic state. In the absence of a suitably reactive substrate intersystem crossing to the triplet (PhN) or diradical nitrene species occurs. Such decompositions are well-documented,⁶ and are generally achieved in solution at moderate temperatures, ($120\text{--}160^\circ\text{C}$) and have an $E_{\text{act.}}$ of $120\text{--}160 \text{ kJ mole}^{-1}$.

However, aryl azides bearing an ortho unsaturated group decompose at lower temperatures ($80\text{--}100^\circ\text{C}$) and show a significantly lower $E_{\text{act.}}$ of $80\text{--}120 \text{ kJ mole}^{-1}$. Examples of this latter type are the formation of benzofuroxan (42) from o-nitrophenyl azide, 2,1-benzisoxazoles (43) from o-azido-ketones and 2H-benzotriazoles (44) from o-azidoazo-compounds as exemplified in reactions (i-iii).



These cyclisations are also noteworthy in that they are free from azo-compound and amine by-products that generally accompany nitrene-mediated aryl azide decompositions.

It is now realised, from kinetic evidence,^{19,20} that such azide decompositions proceed via an assisted nitrogen loss from the azide rather than by a discrete nitrene intermediate. Of the two mechanisms proposed that involving a 6π -pericyclic process, as favoured by Dyll,¹⁹ and as outlined in Scheme 12 for *o*-azidoaryl ketones, is most likely.

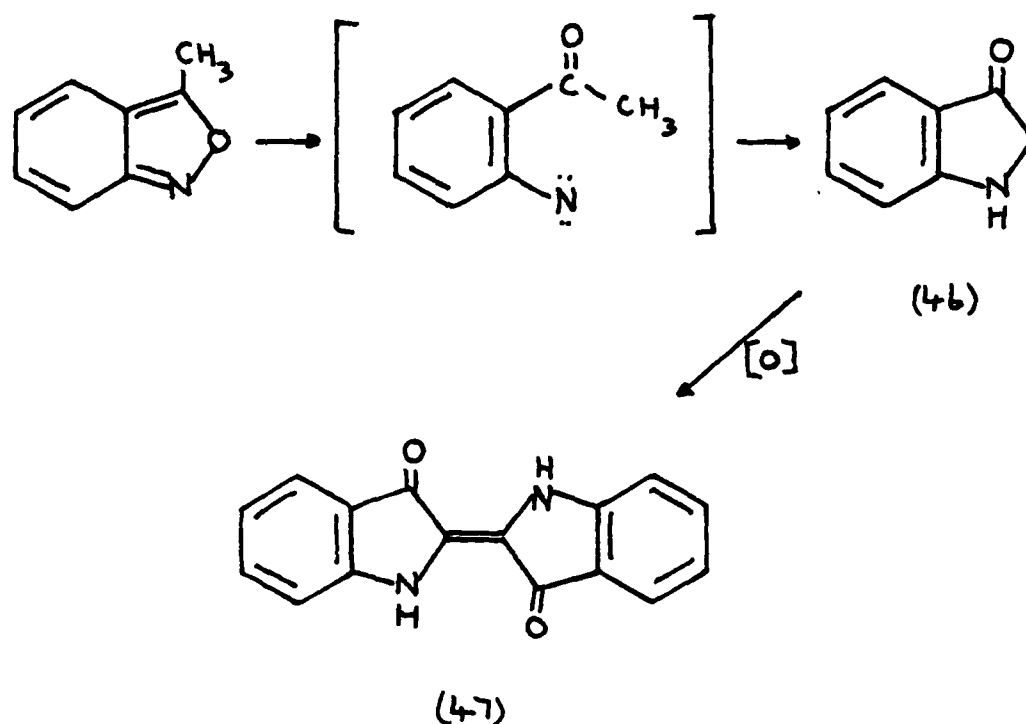


Scheme 12

Consequently, the generation of, for example, *o*-nitrenoaryl ketones is not possible directly from aryl azides, and indirect routes have to be employed. One method of particular interest, is the formation of *o*-nitreno ketones by the thermolysis and photolysis of 2,1-benzisoxazoles; the photo-induced ring-expansion of 3-alkyl-2,1-benzisoxazoles to 3H-azepines,²¹ and the thermal rearrangement of 3-aryl- and 3-heteroaryl-2,1-benzisoxazoles to acridones and related systems²² being typical examples.

We were intrigued, however, by a little-known report²³ that

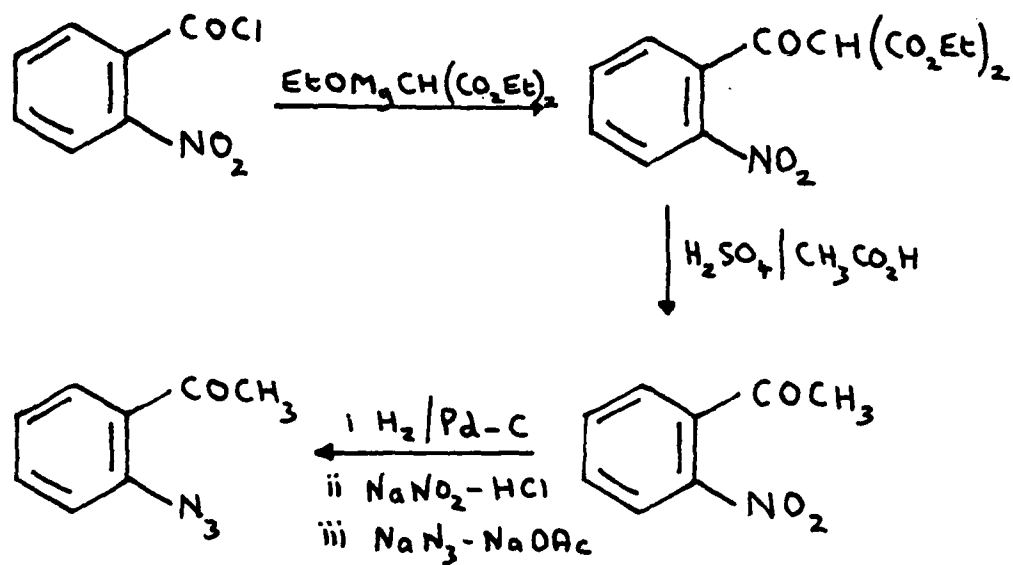
3-methyl-2,1-benzisoxazole (45), on strong heating (250°C) yields indoxyl (46). This rearrangement presumably involves cleavage of the O-N bond and subsequent insertion of the nitrene so formed into the proximate methyl group.



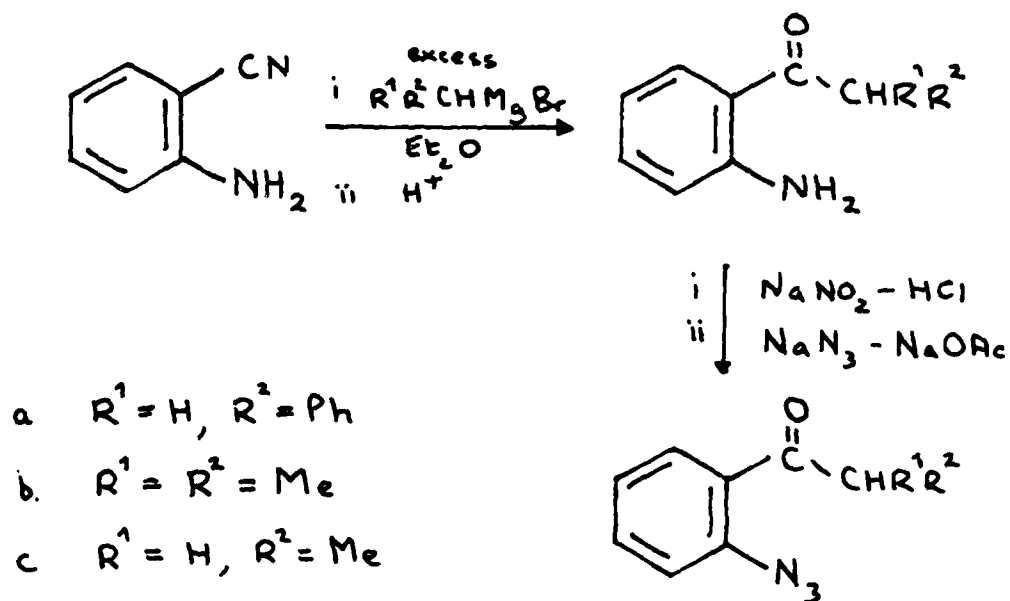
We have repeated this reaction under spray pyrolysis conditions and can confirm that at 300°C 3-methyl-2,1-benzisoxazole (45), and *o*-azido acetophenone (prepared as indicated in Scheme 13) both yield, initially, indoxyl (46). Not unexpectedly, however, exposure of the product to air brings about a rapid dimerisation and oxidation of (46) to indigo (47), which was isolated in 15% yield overall.

This result prompted the preparation of other *o*-azidoaryl alkyl ketones (48) (Scheme 14)²⁴ and an investigation of their thermolysis and spray pyrolysis products.

As expected, the azidoisopropyl ketone (48b) in boiling xylene (140°C) gave only 3-isopropyl-2,1-benzisoxazole (49) (yield > 90%). Similarly, on spray pyrolysis at 300°C - only (49) was obtained.

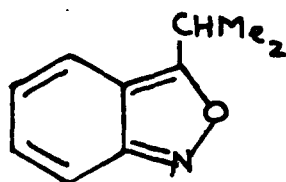


Scheme 13

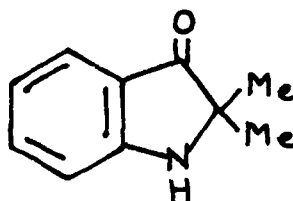


Scheme 14

However, spray pyrolysis of the azide (48b) or the 2,1-benzisoxazole (49) at 420°C gave 2,2-dimethylindoxyl (50) in excellent yield (89%).

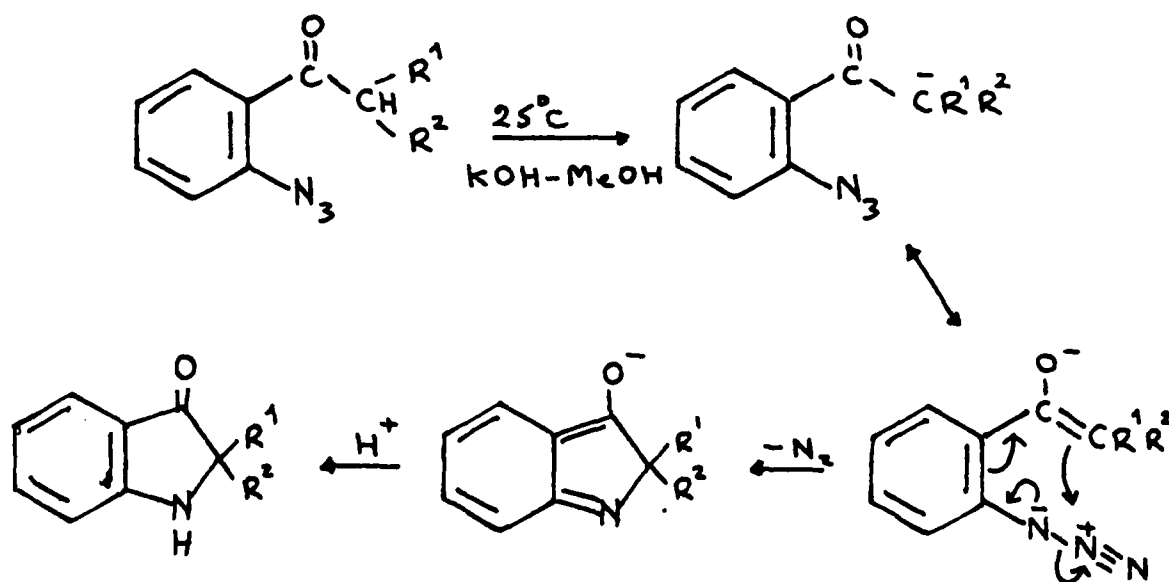


(49)



(50)

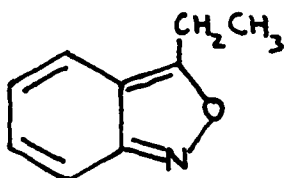
This procedure has some merit as a preparative route to the not so readily accessible 2,2-disubstituted and 2,2-spiro-indoxyls, and complements the method recently described,²⁵ in which o-azidoaryl-sec-alkyl ketones under basic conditions undergo an assisted loss of nitrogen from the enolate ion as exemplified in Scheme 15.



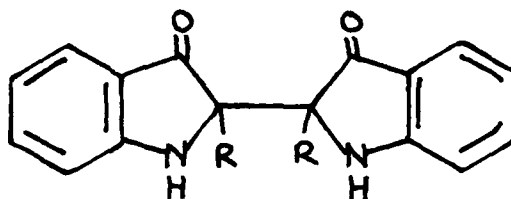
Scheme 15

Although, 2,2-disubstituted indoxyls are stable, the 2-mono-substituted derivatives, like indoxyl itself, readily dimerise. It was of interest, therefore, to study the thermolysis of the primary alkyl ketones, (48a) and (48c).

o-Azidopropiophenone (48c) at 350°C gave only 2,1-benzisoxazole (51; 87%). However, at higher temperatures (420°C) in addition to the 2,1-benzisoxazole a low yield (3%) of a dimer (52; R = Me), identical to that reported by Hassner and Haddadin,²⁶ was isolated.



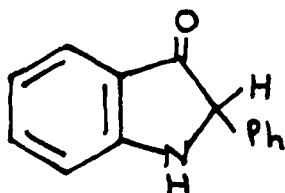
(51)



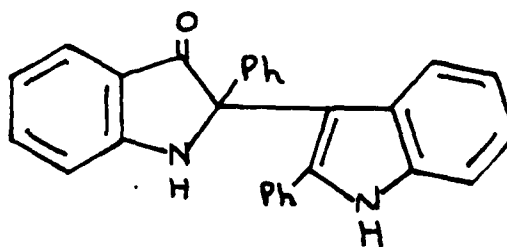
(52)

The benzyl ketone (48a) on thermolysis (boiling xylene) or on spray pyrolysis at 300°C, gave only 3-benzyl-2,1-benzisoxazole. However, at 400°C, two products were obtained, neither of which corresponded to the dimeric structure (52; R = Ph), described by Hassner and his co-worker.²⁶

Neither of these products has as yet been identified unequivocally. The minor product (4%), m.p. 203°C, displays $\nu(\text{C=O})$ and $\nu(\text{NH})$ as sharp intense peaks at 3390 and 1660 cm^{-1} , respectively, and has a molecular formula $\text{C}_{14}\text{H}_{11}\text{NO}$, as determined by elemental analysis and mass spectrum (m/z 209). The mass spectral fragmentation pattern shows loss of 2H, CO, HCN and C_6H_5 fragments. These data are consistent with the 2-phenylindoxyl structure (53), but more conclusive proof of identity is required, as indoxyl (53) is reported²⁷ to be an unstable yellow solid, m.p. 147°C.



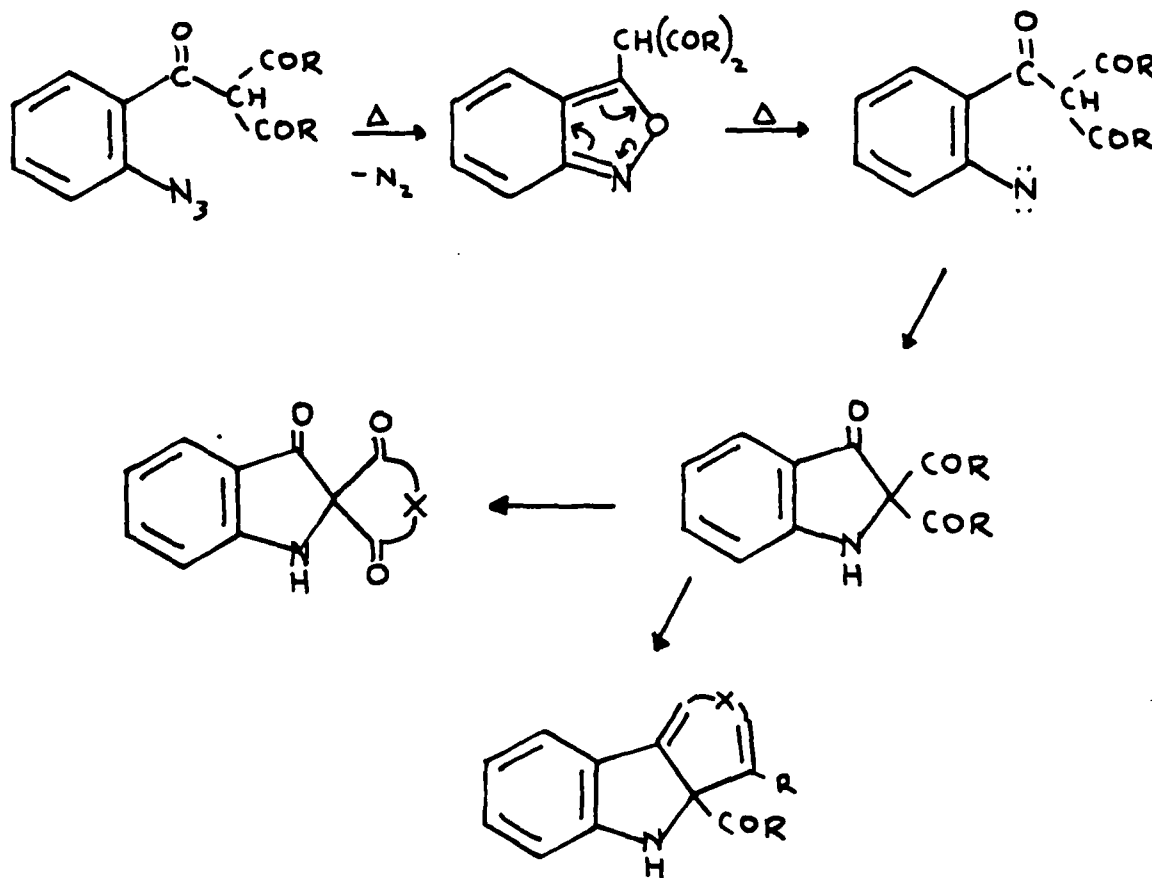
(53)



(54)

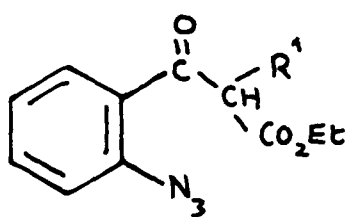
The major product, isolated in 25% yield as a yellow crystalline solid, m.p. 244°C has $m/z = 400$ mass units, corresponding to a molecular formula $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}$, and would appear to be a condensation product of the minor product, rather than the dimer (52; $\text{R} = \text{Ph}$), m.p. 182°C .²⁸ A possible structure is the 2-phenyl-2-(3-indolyl)-indoxyl (54). The p.m.r. spectrum shows only NH and aromatic protons (in the ratio of 1:9) and the i.r. spectrum has $\nu(\text{NH})$ at 3350 and $\nu(\text{C}=\text{O})$ at 1695 cm^{-1} . The mass spectrum is consistent with a structure of this type with losses of H , CO (M^+) and C_6H_5 .

Attention was next directed to the synthesis of more highly functionalised *o*-azidoaryl ketones in an attempt to produce 2,2-disubstituted indoxyls suitable for further modification to fused tricyclic systems, as for example in Scheme 16.

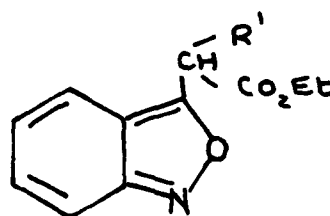


Scheme 16

Accordingly, *o*-azidobenzoyl derivatives of diethyl malonate (55a), ethyl acetoacetate (55b), and ethyl benzoylacetate (55c) have been prepared as outlined in Scheme 13 (*o*-azidobenzoyl chloride in place of the *o*-nitro-compound). Ethyl α -(*o*-azidobenzoyl)phenylacetate (55d) was prepared by treating ethyl phenylacetate, successively at -78°C , with lithium *N*-isopropylcyclohexylamide and *o*-azidobenzoyl chloride.



(55)



(56)

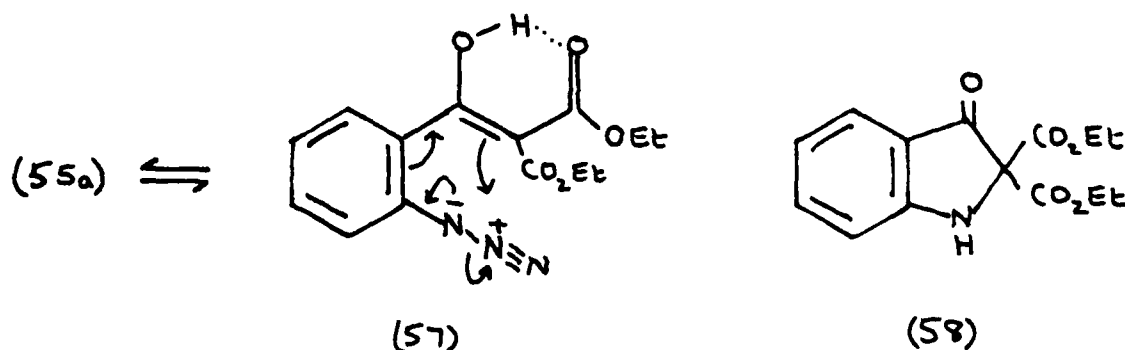
- a $\text{R}' = \text{CO}_2\text{Et}$
- b $\text{R}' = \text{COCH}_3$
- c $\text{R}' = \text{COPh}$
- d $\text{R}' = \text{Ph}$

The products from thermolyses and pyrolyses of these azides have proved to be unpredictable and have yielded several types of interesting structures, some of which have not yet been fully characterised.

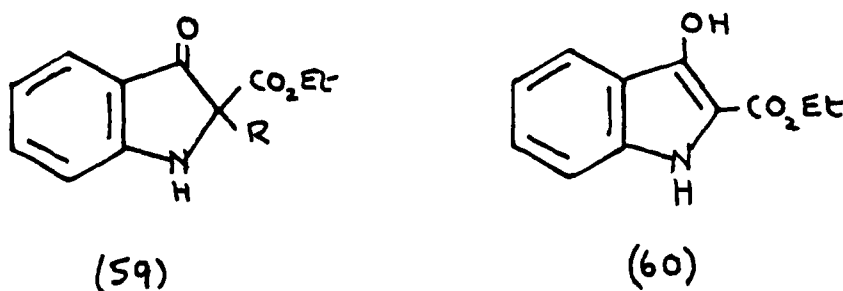
The most simple decomposition proved to be the malonate derivative (55a). Thermolysis in boiling xylene (140°C) or *o*-dichlorobenzene (178°C) in contrast to the *o*-azidoaryl alkyl ketones (48) gave not the expected 2,1-benzisoxazole (56a) but 2,2-diethoxycarbonylindoxyl (58) in excellent yield ($> 80\%$). Spray pyrolysis of the diester was less efficient and gave the indoxyl in only 17% yield along with much tar.

A plausible explanation for this unexpected result became apparent on examination of the p.m.r. spectrum of the azidobenzoyl malonate. In keeping with other known²⁹ unsubstituted benzoyl malonates the diester

exists mainly (55:45) as the intramolecularly hydrogen bonded enol form (57) [δ CDCl_3 , 13.5 (s, OH); 5.5 (s, CH)]. Hence, we suggest, that on thermolysis the azide has an alternative mode of cyclisation via a pericyclic reaction with the alkene bond of the enol to give the fully benzenoid heterocycle (58), a process which competes successfully with formation of the less stable *o*-quinonoid 2,1-benzisoxazole. Kinetic data support this view in that the reported $E_{\text{act.}}$ for Equation (11) is 110 kJ mole^{-1} ,² whereas preliminary kinetic results³⁰ for thermolysis of the azidomalonate in toluene indicate an $E_{\text{act.}}$ of ca. 80 kJ mole^{-1} .



A similar situation prevails with the (azidobenzoyl)phenyl acetate (55d). Its p.m.r. spectrum indicates that the azide exists mainly (66:33) as the enol form, and on thermolysis it yields indoxyl (59; R = Ph) rather than the 2,1-benzisoxazole (56d).



Different modes of cyclisation were observed in the thermolysis of the acetoacetate and benzoyl acetate derivatives.

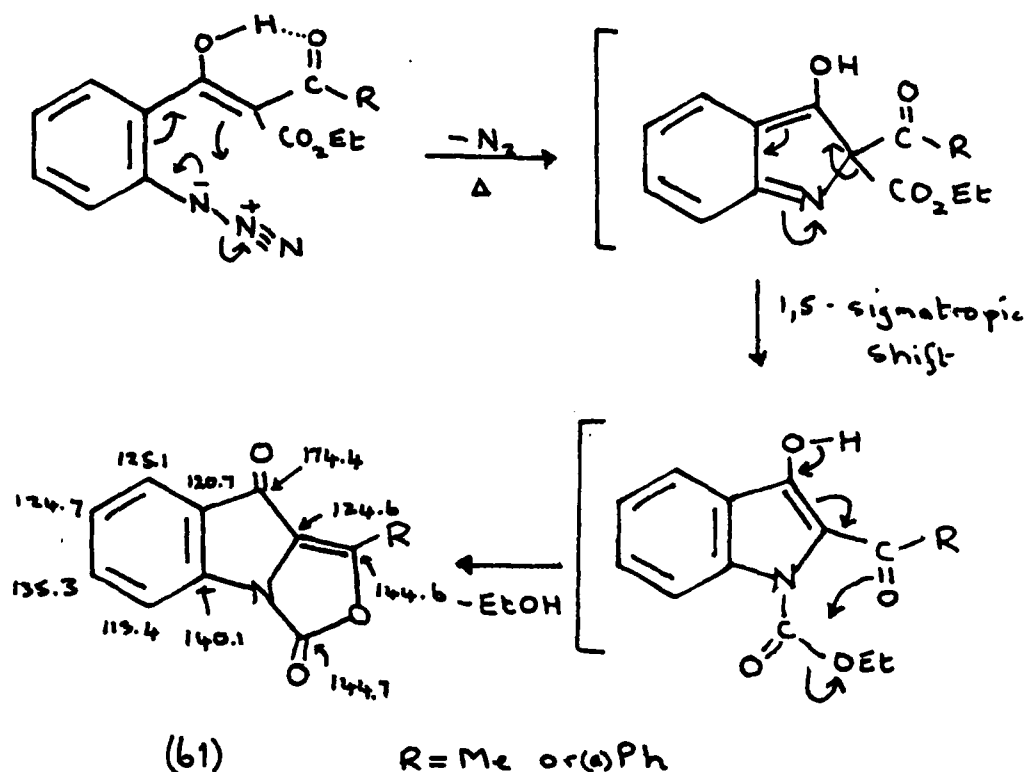
Thermolysis of the azidoacetoacetate (55b) in toluene gave the 2,1-benzisoxazole (56b) along with a yellow crystalline material, m.p. 189°C (26%). However, on thermolysis at higher temperature (boiling o-dichlorobenzene - b.p. 178°C) or on spray pyrolysis no 2,1-benzisoxazole was isolated. In the former case the yellow product, m.p. 189°C was obtained in 29% yield, accompanied by an indoxyl (from i.r. and p.m.r. evidence) (34%) that was obviously not (no acetyl group) the anticipated structure (59; R = COCH₃). This product was subsequently identified as the known ethyl 3-hydroxyindole-2-carboxylate (60), m.p. 120°C (Lit.³¹, m.p. 121°C). Spray pyrolysis of (55b) yielded the same two products but in much reduced amounts (2% and 6%) respectively.

In contrast, the azidobenzoyl acetate (55c) on thermolysis in boiling xylene (140°C) or on spray pyrolysis (350°C) gave as sole product a yellow crystalline material, m.p. 222°C, in 69% and 39% yield, respectively. The spectra (i.r., p.m.r.) and analytical data for this compound were inconsistent with either a 2,1-benzisoxazole or an indoxyl structure, but resembled closely those shown by the unknown yellow product obtained by decomposition of the acetoacetate derivative (55b). For example, both show two carbonyl groups $\nu(\text{C=O})$ at 1780-1850 (vinyl ester or lactone) and 1695-1700 cm^{-1} (ketone) with further absorption at 1640-1660 cm^{-1} (C=N or C=C?). The p.m.r. spectrum of the acetoacetate product shows only a singlet CH₃ and aromatic protons, whereas the benzoylacetate product has only aromatic protons. Clearly there has been a loss of the ethyl ester group, and this is confirmed by the mass spectra which in each case show a molecular ion corresponding to a loss of N₂ and EtOH from the parent azide, i.e. M⁺ 201 and M⁺ 263 respectively as the base peaks. The mass spectra are in agreement with the elemental analyses and indicate molecular formulae of C₁₁H₇NO₃ (acetoacetate product) and C₁₆H₉NO₃ (benzoylacetate product).

On the basis of spectral and analytical data the oxazolo[3,4-a]

indole-2,8-dione structures (61; R = Me or Ph) have been assigned tentatively to these products.

The mode of formation of these novel and unexpected ring-systems is not yet clear, but must involve a migration of the ethoxycarbonyl group from carbon to nitrogen. Subsequent enolisation of the benzoyl group and cyclisation with displacement of ethoxide in the manner suggested in Scheme 17 would yield the tricycles (61).

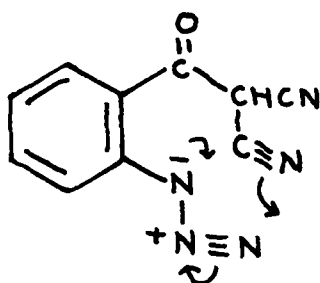


Scheme 17

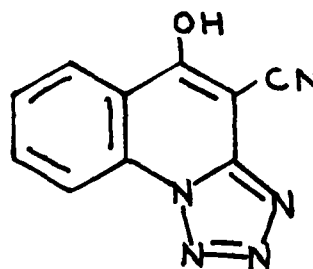
However, any mechanistic rationale must remain speculative until unequivocal proof of structures for (61) is obtained.

Unfortunately, conclusive proof of structure by X-ray analysis has been thwarted so far by the lack of success in producing suitable crystals.* Further work on the unambiguous synthesis and chemistry of those hitherto unknown heterocyclic systems (only two previous examples reported³²) is being undertaken.

An anomalous result was also obtained on thermolysis of the o-azidobenzoylmalononitrile (62). Decomposition in boiling toluene, xylene, or bromobenzene furnished a single product, which, despite the absence of the characteristic $\nu(\text{N}_3)$ at ca. 2120 cm^{-1} in the i.r. spectrum, had the same molecular weight (mass spectrum) as the starting azide. Clearly, nitrogen loss had not occurred; spectroscopic and analytical evidence were in accord with the cyanotetrazolo[5,1-a]-quinoline (63) formed by intramolecular 1,3-dipolar cycloaddition of the azide with the pendant cyano group. Analogous cycloadditions involving o-azidocinnamonnitriles³³ and o-azidoaryl allyl ethers³⁴ have been noted previously.



(62)



(63)

* Note added in proof.

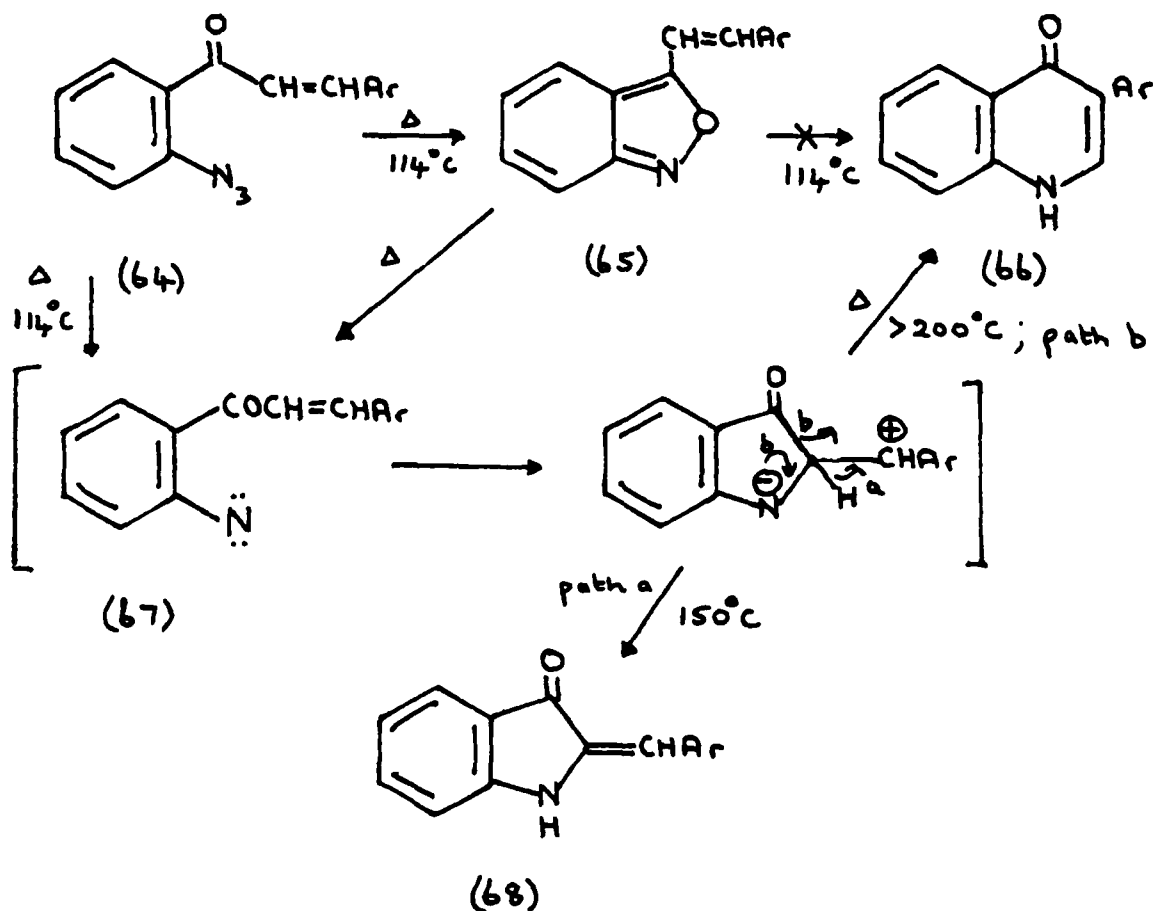
The 500 MHz P.m.r. and the ^{13}C n.m.r. spectra have recently been obtained⁺ and are in accord with structure (61). ^{13}C n.m.r. chemical shifts are appended to structure (61a).

⁺ We thank Dr. O. Meth-Cohn, National Chemical Research Laboratory, C.S.I.R., P.O. Box 395, Pretoria 0001, South Africa, for these measurements.

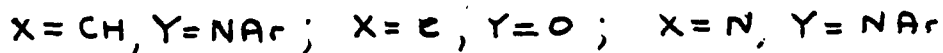
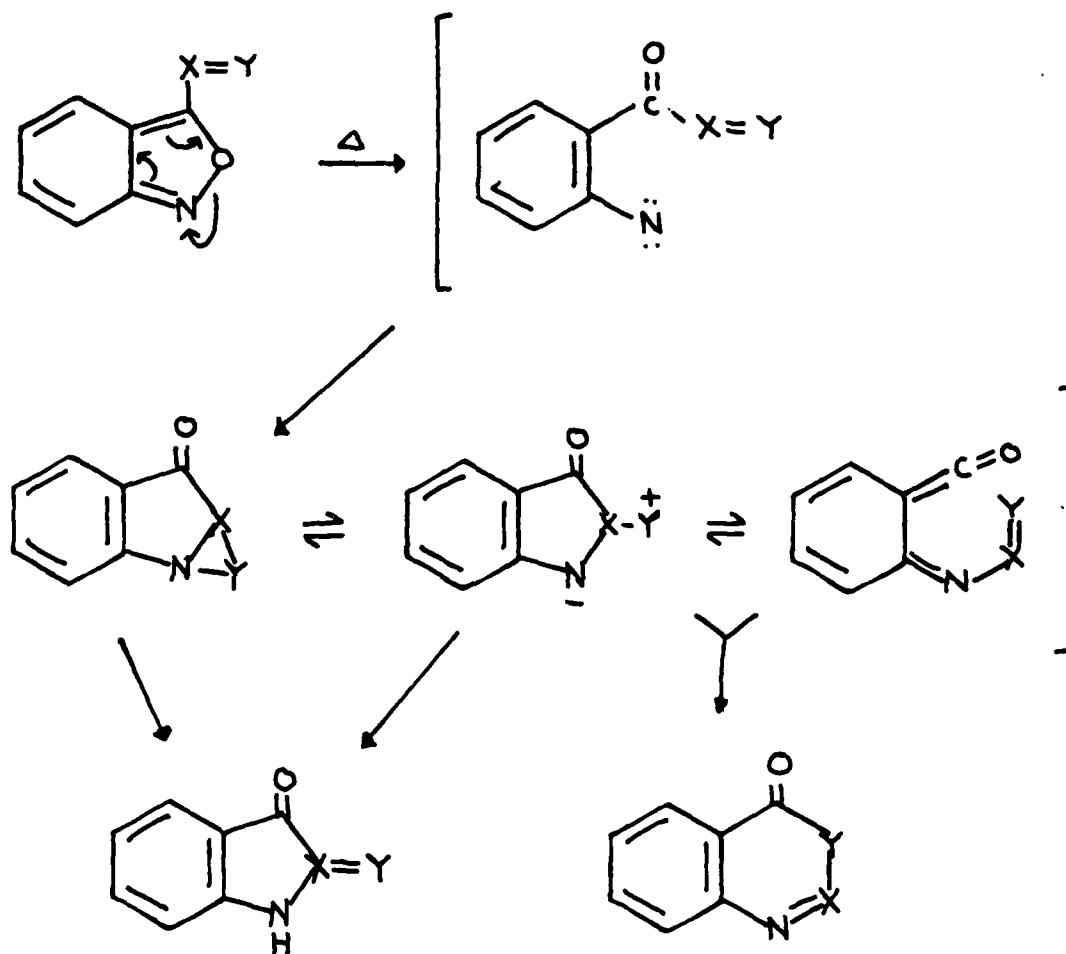
Section 6

Thermolysis and Spray Vacuum Pyrolysis of 2,1-Benzisoxazoles
bearing an Unsaturated 3-Substituent

In a preliminary publication^{35a} we have shown that o-azido chalcones (64), prepared by base-catalysed condensation of o-azidoacetophenone with an aryl aldehyde, on thermolysis in boiling toluene, yield mainly the expected 3- β -styryl-2,1-benzisoxazoles (65) along with minor amounts (5-10%) of 3-aryl-4-quinolones (66). Further investigation revealed that other products, e.g. 2-arylideneindoxyls (68) were also formed depending on the thermolysis temperature. These products are the result of the formation and subsequent cyclisation of o-nitrenoketone (67) species as outlined in Scheme 18.



Extension of this rearrangement process to other 2,1-benzisoxazoles with 3-unsaturated substituents containing hetero-atoms, was successful^{35b} and prompted us to propose a new general reaction sequence as outlined in Scheme 19.

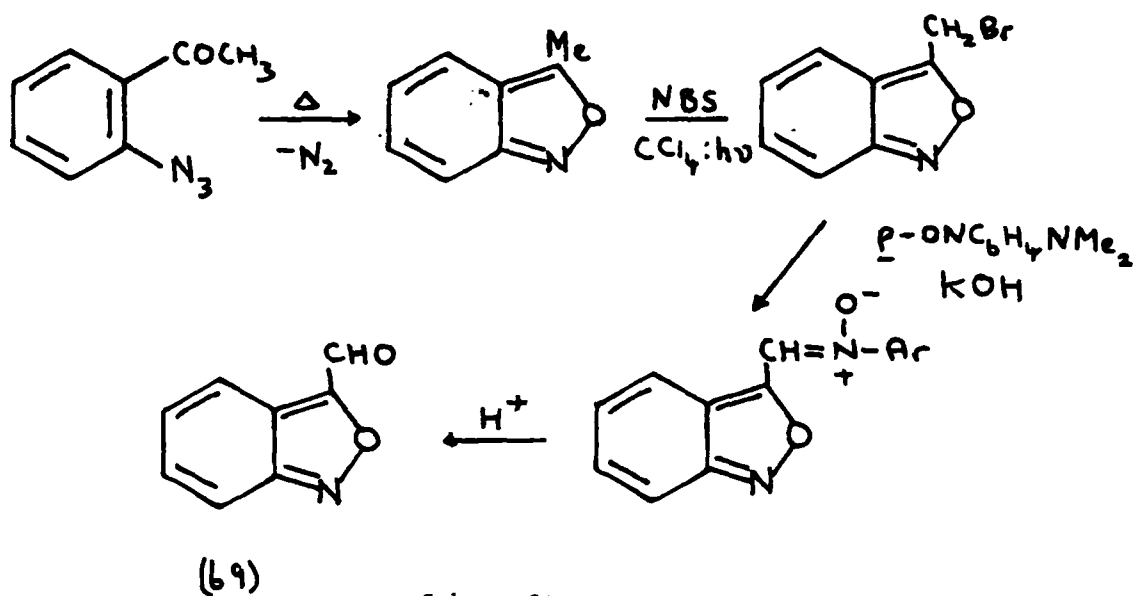


Scheme 19

We now report on further examples of these novel transformations.

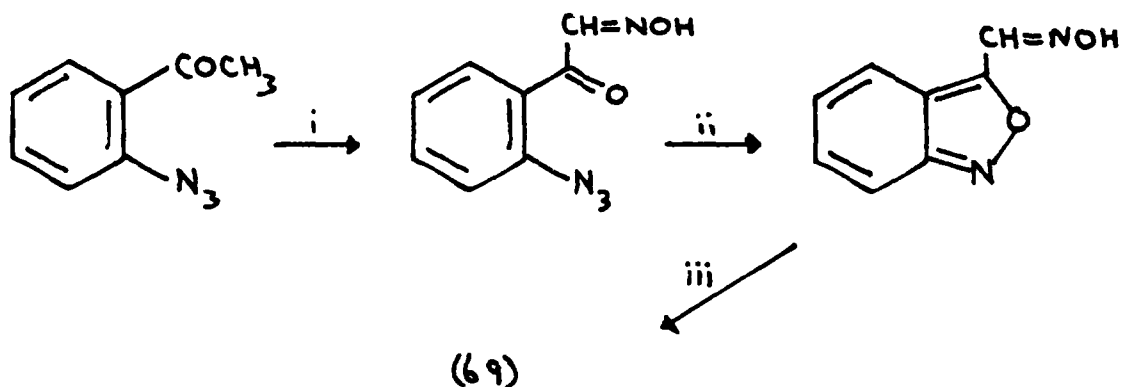
The key intermediate for the synthesis of the required 3-substituted 2,1-benzisoxazoles was the aldehyde (69). The previous method³⁶ was tedious and in our hands unreliable. Hence, two new procedures have been developed. The first (Scheme 20), based on the Kröhnke aldehyde synthesis, gave the aldehyde in 30-40% overall yield.

This was preferred to the second route illustrated in Scheme 21, which,



Scheme 20

although giving excellent yields in the thermolysis and oxime hydrolysis stages, suffered from poor oxime yields from the initial nitrosation step.



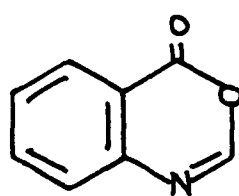
Reagents: (i) $C_5H_{11}ONO$; HCl; (ii) Δ , $140^\circ C$, xylene; (iii) pyridinium dichromate.³⁷

Scheme 21

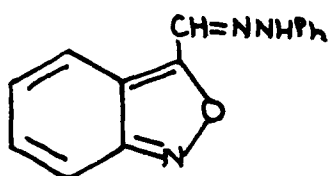
Spray vacuum pyrolysis ($350^\circ C$) or solution thermolysis (boiling 1-methyl naphthalene b.p. $245^\circ C$) of the aldehyde (6) was disappointing in that only tarry products were obtained, rather than the hoped for

(on the basis of Scheme 19), 3,1-benzoxazinone (70). Similarly, only intractable materials were obtained on thermolysis of the oxime and semi-carbazone derivatives of aldehyde (69).

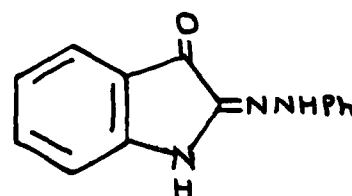
In contrast, decomposition of the phenylhydrazone (71) in boiling *o*-dichlorobenzene was complete in 10 minutes and gave the isatin monophenylhydrazone (72) (54%), m.p. 135°C (Lit.³⁸, 135°C) as the sole identifiable product.



(70)

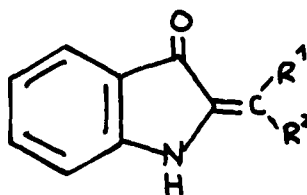
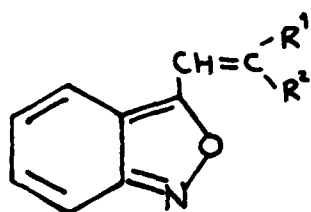


(71)

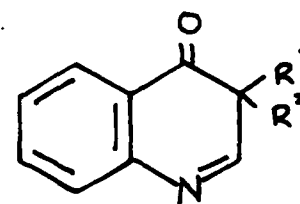


(72)

In a similar manner, the Knövenagel condensation products (73a) and (73b) respectively, of aldehyde (6) with diethyl malonate and with malononitrile on thermolysis (at 240°C) gave only the indoxyl derivatives (74a) and (74b).



(74)

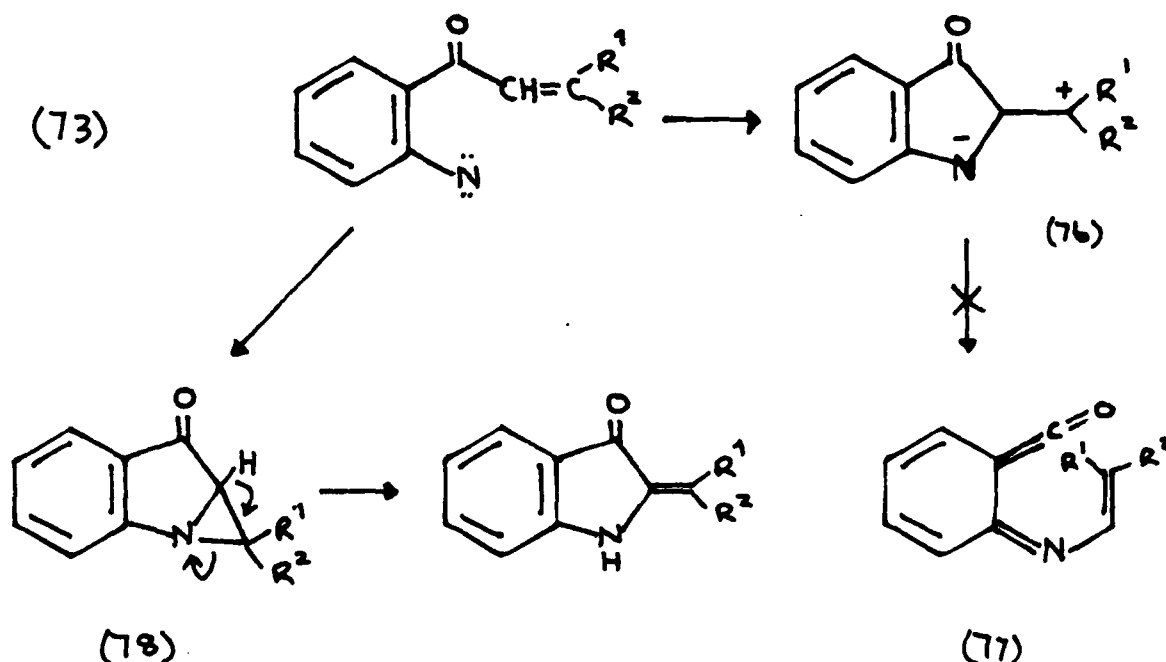


(75)

- (73) a $R^1=R^2=CO_2Et$
 b $R^1=R^2=CN$
 c $R^1=CO_2Et$, $R^2=COCH_3$
 d $R^1=CO_2Et$, $R^2=COPh$

The absence in these decompositions of novel quinolones of type (75), as predicted on the basis of the mechanism outlined in Scheme 19 is disappointing, but presumably is related to the stability of the

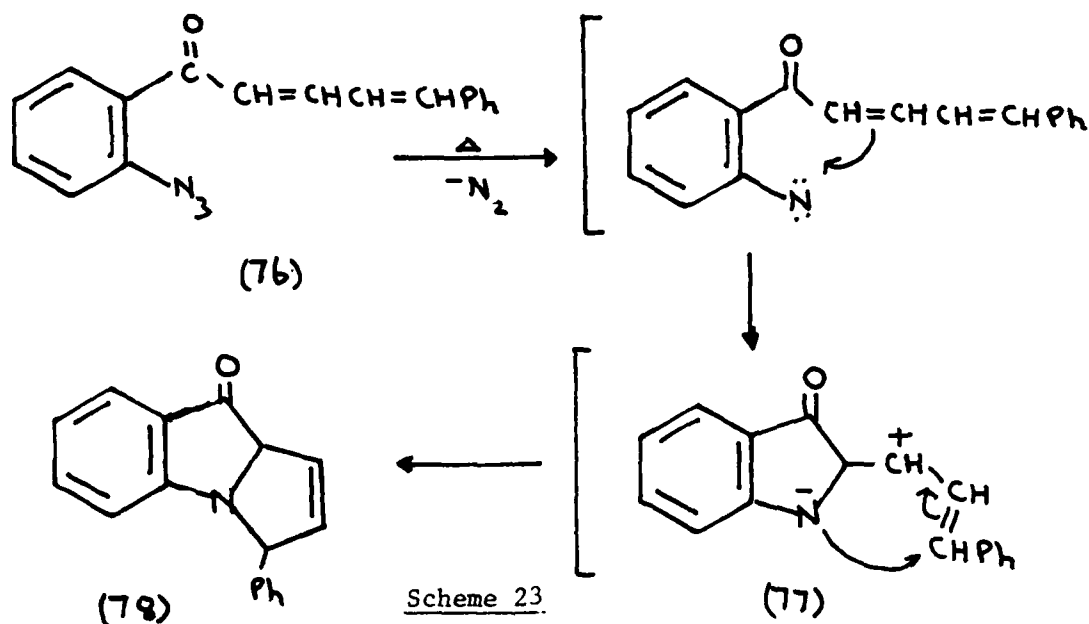
intermediates (76) (Scheme 22), which undergo rapid proton transfer to furnish indoxyls (74) rather than ring-cleavage to iminoketenes (77), the quinolone precursors. In fact, the participation of the charged intermediate (76) bearing two strongly electron-withdrawing groups is questionable, and a more likely route to the indoxyls is via the tricyclic aziridine intermediates (78).



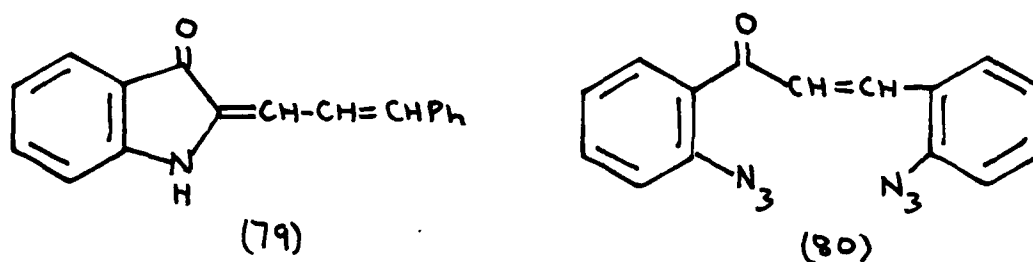
Scheme 22

The condensation products (73c) and (73d) of aldehyde (69) with ethyl benzoylacetate and ethyl acetoacetate on thermolysis gave only tars.

Interesting extensions of these thermal rearrangements concerned the cimmamoyl derivative (76) and the diazidochalcone (80). A likely product from the thermolysis of (76) would be tricycle (78), a possible mitomycin³⁹ analogue precursor, formed by intramolecular conjugate addition of a charged intermediate (77) to the indoxyl system as illustrated in Scheme 23.



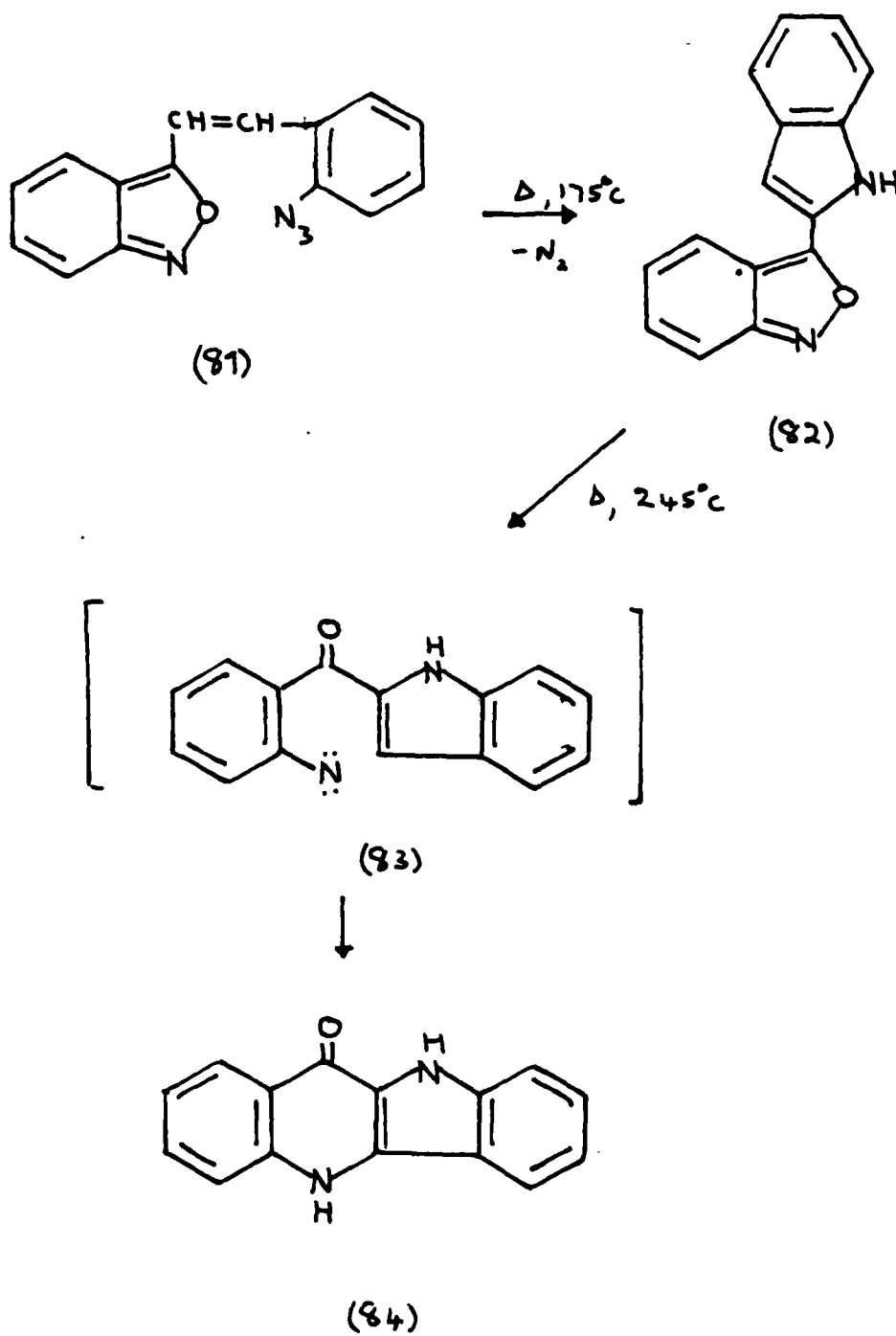
In the event, however, only the 2-cinnamylidene indoxyl (79) was isolated.



As expected, the diazide on thermolysis in boiling toluene (114°C) gave the styryl anthranil (81), via an assisted nitrogen loss. Further heating at 175°C , (boiling *o*-dichlorobenzene) brought about non-assisted decomposition of the second azide, followed by addition of the resulting nitrene to the double band, to give ultimately the indoloanthranil (82). This product now represents an example of a 2,1-benzisoxazole bearing an unsaturated 3-substituent and, as such, should rearrange at higher temperatures, via the nitrenoketone, (83) in accord with Scheme 19. In fact, in boiling 1-methylnaphthalene (b.p. 245°C) the nitrene was produced, presumably as the singlet electrophilic species, which substituted at the nucleophilic

3-position of the indole nucleus to give the tetracyclic system (84)

(40%) m.p. $> 350^{\circ}\text{C}$ (Lit.⁴⁰ $> 330^{\circ}\text{C}$).



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APPENDIX A

Cyclisations of Azidoformates; Formation of Azepine Dimers

By OTTO METH-COHN* and SALAH RHOUDI

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Summary Pyrolysis of benzyl azidoformate at 300–350 °C gave an oxazolo[3,4-*a*]azepin-2-one which spontaneously dimerised by [6 + 4] *exo-anti*-cycloaddition,

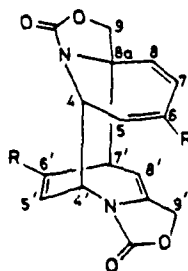
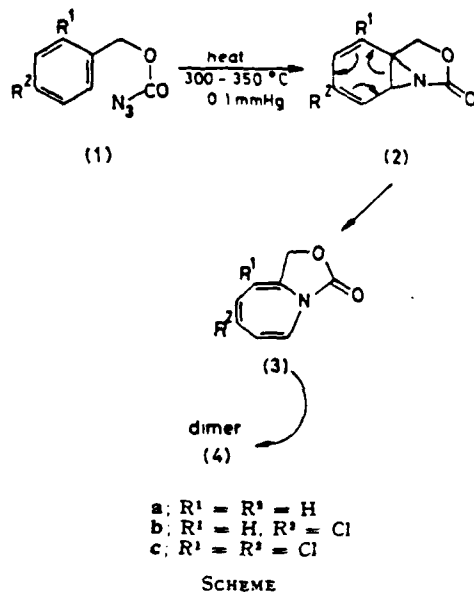
while the 2,4-dichlorobenzyl ester gave the isomeric *syn*-dimer; the 4-chlorobenzyl azidoformate gave a 3:2 mixture of the *anti*- and *syn*-dimers.

ALKYL and aryl azidoformates decompose in hot benzene to give azepines, by way of cheletropic addition of the nitrene.¹ Furthermore, these 1*H*-azepines undergo [6 + 4] dimerisation on heating to 120–130 °C to give *exo*-dimers.² We report herein the first example of an intramolecular ring-expansion of a benzene to an azepine, which because of its considerable planarity undergoes spontaneous dimerisation in a highly selective manner.

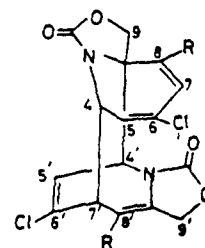
When benzyl azidoformate (1a) is sprayed in *vacuo* through a hot tube (15 × 2 cm) a crystalline azepine dimer forms in the condenser (Scheme) which recrystallises from bis-[2-methoxyethyl] ether (80%). Azepine dimers were also obtained from 4-chlorobenzyl azidoformate (1b) and from 2,4-dichlorobenzyl azidoformate (1c) (69 and 58%, respectively).

The dimers showed characteristic carbonyl absorption frequencies for an isolated oxazolidone and a conjugated oxazolidone (ν 1760 and 1700 cm⁻¹) in their i.r. absorption spectra, and molecular ions together with evidence of retro-cycloaddition in their mass spectra.[†] However, their 300 MHz ¹H n.m.r. spectra were particularly definitive giving almost first-order spectra, which, after extensive decoupling allowed unambiguous assignment of their structures.

The parent azepine-dimer (4), formed from (1a), as with the 1-ethoxycarbonylazepine dimer,² is formed by a *peri*-, site-, and regio-specific [6 + 4] cycloaddition to which we assign an *exo-anti*- (*anti* refers to the relative disposition of the fused 5-membered rings) structure. From the 4-chlorobenzyl azidoformate (1b) was obtained a 3:2 mixture of the isomers (5) and (6) (i.e. the *anti*- and *syn*-dimers of [6 + 4] *exo*-dimerisation of the corresponding azepine). One isomer (6) was separated by column chromatography (on



(5) R = H, mp 139–140 °C
(6) R = Cl, mp 204 °C



(7) R = H, mp 222 °C
(8) R = Cl, mp 230–234 °C

silica with diethyl ether elution) while the other was purified by preparative h.p.l.c. [25 × 2.54 cm stainless steel column dry-packed with Lichroprep Si 60 (15–25 μm) (E. Merck), solvent: iso-octane-ethyl acetate (4:1), 5.04 ml/min]. 2,4-Dichlorobenzyl azidoformate (1c) indicated another aspect of specificity in that the derived nitrene attacked solely the 1,6-bond of the benzene ring, rather than the 1,2-bond, giving the azepine (3c). The dimer obtained

TABLE. Chemical shifts (^1H .n.m.r.) of the azepine dimers (4)–(7).

Proton	(4) [$^2\text{H}_6$]DMSO ^a		Compound (Solvent)		(6) (CDCl_3)		(7) (CDCl_3)	
	δ	$J/\text{Hz}^{b,c}$	(5) (CDCl_3)	$J/\text{Hz}^{b,d}$	δ	$J/\text{Hz}^{b,e}$	δ	$J/\text{Hz}^{b,f}$
9	4.07d	9 (9,9)	4.40s		4.13d	9 (9,9)	4.57d	10 (9,9)
8	4.39d				4.20d		4.77d	
7	5.8–6.1m		6.13d	12 (7,8)	6.09d	12.5 (7,8)	—	
6	5.8–6.1m	8 (5,6)	5.67d		5.53d		6.52s	
5	5.09t	8 (4,5)	5.92d	6.5 (4,5)	6.12d	6.5 (4,5)	6.47d	7 (4,5)
4	5.21t	6 (4,4')	5.33t	7.5 (4,4')	5.22t	8.5 (4,4')	5.35t	8 (4,4')
9'	4.64d	13 (9',9')	4.79 ca. d		4.79 ca. d	14 (9',9')	4.87d	15 (9',9')
8'	4.80d						5.02d	
7'	4.42d	9.5 (7',8')	4.47d	9 (7',8')	4.38d	9 (7',8')	—	
6'	3.15t	9.5 (6',7')	3.34d		3.71t		4.13s	
5'	6.24t	9.5 (5',6')	—		—		—	
4'	5.8–6.1m	11 (4',5')	6.05d	9 (4',5')	6.00d	9 (4',5')	6.27d	9 (4',5')
	5.66d		5.18t		4.50d		5.30d	

^a DMSO = dimethyl sulphoxide. ^b Coupled protons are given in parentheses. ^c Long-range coupling between 8'–9' is also evident. ^d Long-range couplings between 8'–9' and 5'–7' are evident. ^e Long-range couplings between 8'–9' and 5'–7' are evident. ^f Long-range couplings between 5'–7' and 5–7' are evident.

† The parent dimer (4) showed a strong molecular ion with two successive losses of CO_2 as well as a base peak for the monomer. However, the chloroazepine- and dichloroazepine-dimers (5), (6), and (7) gave successively weaker molecular ions with fragmentation of significance from the monomer only. This involved loss of CO_2 followed by loss of Cl.

therefrom was the *syn*-isomer (7) with no evidence of its *anti*-analogue. Clearly, the mode of dimerisation is delicately dependent upon small changes in the electronic character of the components.

The ^1H n.m.r. data are summarised in the Table. The *syn-anti*-isomerism is particularly clearly defined in the multiplicity of the highest field absorption, due to the homo-enaminic 7'-proton. In the *anti*-series it is bonded to a quaternary 8a-carbon while in the *syn*-isomers the 4-carbon to which it is attached is tertiary. The [6 + 4] mode of addition is also clearly evident, especially from the large

geminal couplings of the 9'-protons (together with the long-range coupling to the 8'-proton, indicating the attachment of an α -*exo*-double bond³) with the smaller coupling for the other geminal 9-protons, and no long-range coupling. The *exo-endo*-specificity is not easy to define on existing data, but n.o.e. studies are underway to confirm the assignments.

We thank the Algerian Government for a grant (to S. R.) and the S.R.C. and Mr. David Moorcroft for 300 MHz n.m.r. spectra.

(Received, 27th August 1980; Com. 935.)

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² L. A. Paquette, J. H. Barrett, and D. E. Kuhla, *J. Am. Chem. Soc.*, 1969, 91, 3616.

³ I. Fleming and D. H. Williams, 'Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, London, 1st Edn., 1966, p. 115.

APPENDIX B

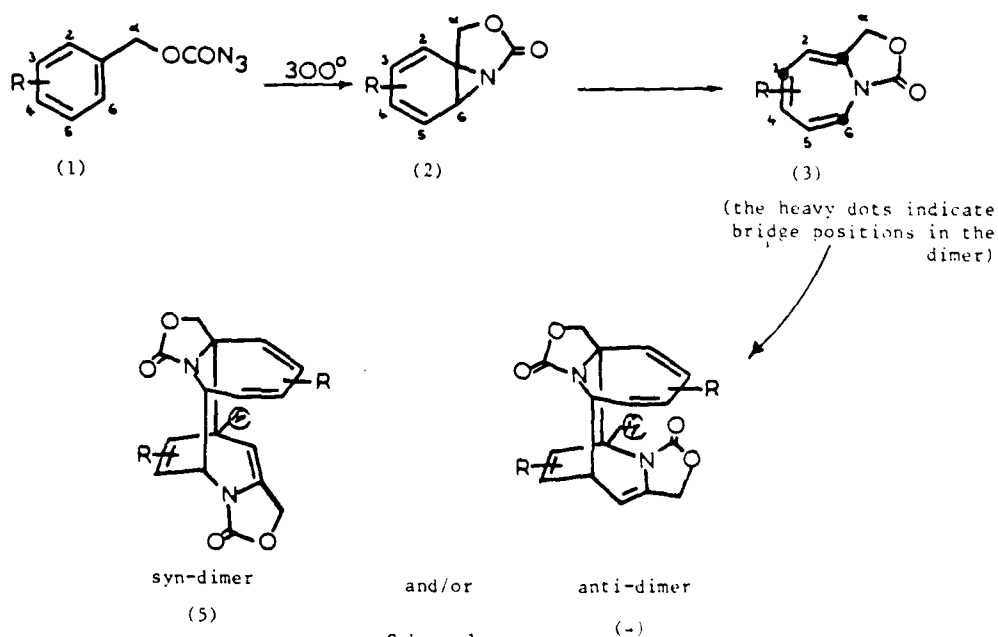
THE INTRAMOLECULAR CHEMISTRY OF BENZYL AND PHENETHYL AZIDOFORMATES

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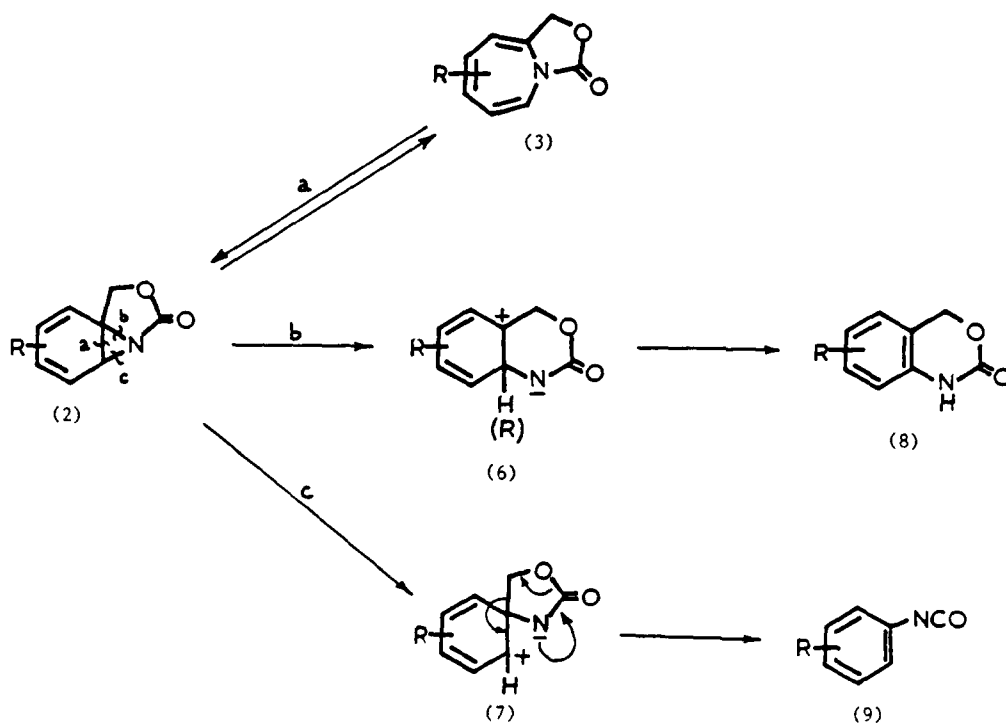
Summary: Benzyl azidoformates yield one of a variety of products on spray pyrolysis dependent upon substitution, including oxazoloazepines, their syn or anti [6 + 4] dimers, their [6 + 6] dimers, a benzoxazinone or an aryl isocyanate; the phenethyl analogues give stable oxazinoazepines.

In an earlier publication¹ we noted that using our new technique of 'Spray Pyrolysis',² benzyl azidoformates (1) were transformed into the dimers (4 and 5) of the oxazoloazepines (3). The reaction was explained by involvement of the tricyclic aziridine (2) (Scheme 1), an intermediate type commonly invoked in nitrene pathways.



Scheme 1

We now report that dependent upon the substituent(s) R, this intermediate (2) has several novel courses open to it (Scheme 2) and that the planar, antiaromatic azepines (3) have other modes of subsequent reaction.



Scheme 2

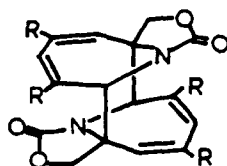
If one considers cleavage of each of the three aziridine bonds of (2) in turn, then the ability of the substituent(s) R to stabilise the positive ionic intermediates (6 and 7) may be seen as the driving force behind these alternative pathways.³

The dimers (4) were obtained from the azides (1) with R = H, 2-Cl, α -alkyl, α -aryl and α -OPh. Similarly, with R = 4-CMe₃, 2,4-Cl₂ or 4-Br the isomers (5) were obtained while in one case (R = 4-Cl) a mixture of both dimers (4 and 5) in a 3:2 ratio was noted. However, the azide (1, R = 2,6-Cl₂) gave a stable, orange azepine (85%) which on further heating (4h, 130°) gave the benzoxazinone (3, R = 2,5-Cl₂) in 64% yield which we explain by way of the equilibrium revealed in Scheme 2, and a 1,2-chlorine shift of intermediate (6, Cl in place of 6-H, R = 2-Cl).⁴

From the azide (1, R = 4-t-butyl) an orange azepine (3, R = 4-t-butyl) was again isolated, dimerisation of which gave the syn isomer (5) only slowly on heating (130°, 4h) due to steric problems. However, the mesityl and durenyl aridoformates (1, R = 2,4,6-Me₃ and R = 2,3,5,6-Me₄ respectively) both yielded unstable azepine monomers (3) which readily and almost

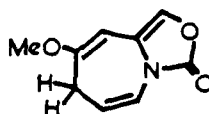
quantitatively were converted into the isocyanates (8 and 9) on brief heating in xylene or merely on standing overnight at ambient temperature. In both of these cases the methyl groups stabilised the positive charge on the ring in the intermediate (7).

In none of the cases in which azepine dimers (4 and 5) were formed, were substituents present at the bridgehead positions (marked by heavy dots in (3)). If such substituents are present, either the dimers are not formed (as with the 2,6-Cl₂, 2,4,6-Me₃ and 2,3,5,6-Me₄ substituted azepines (3) discussed above) or else the dimerisation takes a different course than the [6 + 4] mode. Thus the 3,5-dichlorophenyl- and 3,5-dimethylphenyl azidoformates (1) gave only the symmetrical [6 + 6] dimers (10) on spray pyrolysis. Unlike our [6 + 4] dimers,



(10) a, R=Me (87%)

b, R=Cl (64%)

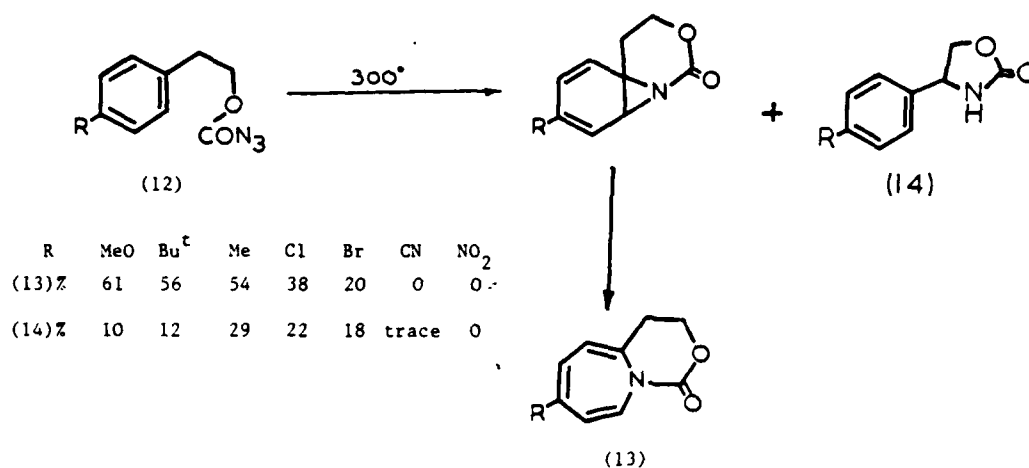


(11)

Paquette and his co-workers⁵ noted that the [6 + 4] dimer of N-ethoxycarbonyl azepine (formed at 130°) rearranged at over 200° to the symmetrical [6 + 6] isomer. Finally, 3-methoxyphenyl azidoformate (1, R = 3-MeO) gave an unseparated mixture of two dimers together with the rearranged azepine (11). These results are all in accord with the known tendency for dimerisations to proceed at the least substituted available sites.⁶

The phenethyl azidoformates (12) behave quite differently on spray pyrolysis. In every case a stable yellow crystalline azepine (13) was isolated which showed no tendency to dimerise or otherwise rearrange thermally, thus underlining the particular instability of the 7/5 fused analogue. In each case the corresponding 4-aryl oxazolidinone (14) was also formed, in amount dependent upon the substituent R, electron releasing groups favouring the azepines.⁷

Acknowledgement: We are indebted to the European Research Office of the U.S. Army for generous financial support. S.R. thanks the Algerian Government for a research grant.



Scheme 2

References and Notes

*All new compounds gave satisfactory analytical and spectroscopic data.

1. O. Meth-Cohn and S. Rhouati, *J.C.S. Chem. Comm.*, 1980, 1162.
2. for details of the method see M. Clancy, D.G. Hawkins, M.M. Hesabi, O. Meth-Cohn, and S. Rhouati, *J. Chem. Research (S)*, 1982, 78.
3. It is possible that the 'intermediates' (6 and 7) may be a crude representation of a transition state of a concerted process or even that homolytic analogues could be involved (cf. ref. 6).
4. As revealed below, azepines with substituents at bridgehead positions of the potential dimers do not dimerise under our conditions.
5. L.A. Paquette, J.H. Barrett and D.E. Kuhla, *J. Amer. Chem. Soc.*, 1969, 91, 3616.
6. L.A. Paquette, D.E. Kuhla and J.H. Barrett, *J. Org. Chem.*, 1969, 34, 2879
7. R.A. Abramovitch, S.B. Hendi and A.O. Kress independently noted the same products in similar yields on flash vacuum pyrolysis of (12, R = H) at 650°. *J.C.S. Chem. Comm.*, 1981, 1087.

APPENDIX C

Spray Pyrolysis: A Powerful New Synthetic Technique†

J. Chem. Research (S),
1982, 78†MICHAEL CLANCY, DAVID G. HAWKINS, MASOUD M. HESABI,
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Flash vacuum pyrolysis has become an important tool in chemistry allowing in particular the synthesis of unstable compounds and trapping of reaction intermediates.¹ Its major limitations are (1) the substrate needs to be capable of volatilisation, thus precluding many potential applications; (2) the method is of value only on a very small scale. These problems are further exacerbated when explosive or thermally unstable substrates are utilised. We have developed a very simple preparative technique that could have wide application and that substantially overcomes the above drawbacks, which we refer to as Spray Pyrolysis. The equipment is illustrated

It should be emphasised that our system, which does not utilise ultra high vacuum but pressures of 0.2–0.5 mmHg, tends to favour the formation of the thermodynamically favoured product, unlike flash vacuum pyrolysis which limits collisions and favours the kinetically controlled pathway.

This method is particularly suited to thermally unstable substrates such as azides, peroxides, and azoalkanes. We have reported elsewhere numerous examples of the application of this technique.⁶

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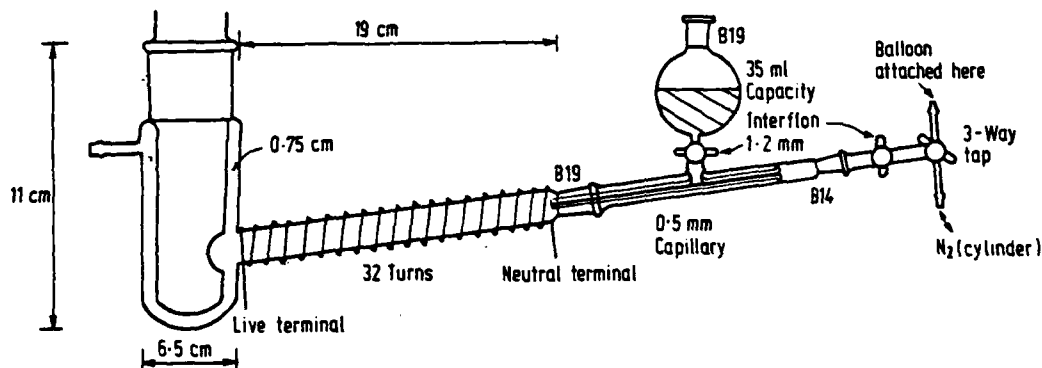


Figure 1 Spray pyrolysis equipment

in Figures 1 and 2. The substrate is introduced into the furnace through a fine-controlled Teflon tap (we use a double-action tap incorporating a fine screw adjustment²) into a capillary tube. A gentle stream of nitrogen (introduced into the capillary through a similar Teflon tap from a balloon) injects the sample as a fine spray into the furnace. The furnace and condenser assembly is best made as a one-piece unit for most purposes. We utilise Nichrome wire³ wound directly onto Pyrex or quartz tubing with the wiring commencing within 0.5 cm of the end of the capillary and continuing to the condenser junction. The wiring is readily cemented on by small blobs of car exhaust cement.⁴ The wire is heated electrically and the temperature controlled by a variable resistance⁵ which was precalibrated.

Using this equipment we regularly pyrolyse samples of 5–10 g which we introduce at 0.5–1 g per hour. Higher rates of introduction are still effective although with either some loss in yield or recovery of unchanged starting material. With solid substrates we have used three methods of handling: (a) with low-melting solids a hair dryer conveniently maintains a molten phase; (b) with solids of m.p. $\leq 100^\circ\text{C}$ (assuming the substrate is stable at its melting point) we use either a steam- or warm water-jacketed inlet system (Figure 2); (c) with less-stable solids we have utilised a mixture of the solid with azobenzene to depress the melting point. Azobenzene is readily removed chromatographically (and any artefacts therefrom) as it is orange and very mobile, is fairly inert, and is low-melting. We have not found solutions to be of any value in pyrolyses.

*To receive any correspondence.

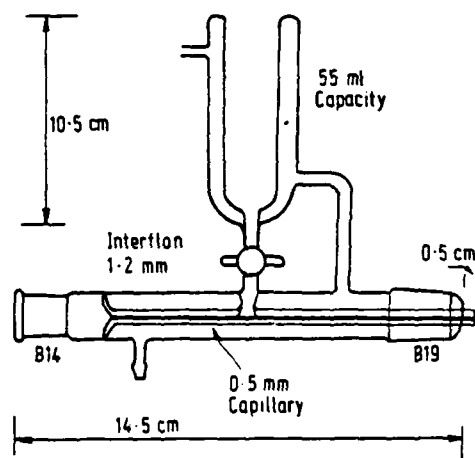
†This is a Short Paper as defined in the Instructions for Authors (*J. Chem. Research (S)*, 1977, Issue 2, p. iv); there is therefore no corresponding material in *J. Chem. Research (M)*.

Figure 2 Apparatus for low-melting solids

References and notes:

¹R. F. C. Brown, 'Pyrolytic Methods in Organic Chemistry,' Academic Press, New York, 1980.²Interflon 1.2 mm Keys supplied by G. Springham and Co. Ltd., Temple Fields, Harlow, Essex.³Flat Nichrome wire (1/32 \times 0.004 in) supplied by Alloy Wire Co. Ltd., Cradley Road, Cradley Heath, Warley, West Midlands, B64 7BP.⁴We use Holts 'Firegum' Car Exhaust Cement available at any car accessory shop.⁵We use a Berco Rotary Regovolt, Type 71A, available from laboratory suppliers.⁶M. Clancy, M. M. Hesabi, and O. Meth-Cohn, *J. Chem. Soc., Chem. Commun.*, 1980, 1112; O. Meth-Cohn and S. Rhouati, *ibid.*, 1980, 1161; 1981, 241.

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$3H$ -Azepines and Related Systems Part 3.¹ Mono- and
Bis- 2-Alkoxy- $3H$ -azepine-3-carboxylates and -3-carboxy-
amides by Photolysis of Mono- and Di- *o*-Azidobenzoyl
Derivatives of Glycols and Diamines. Some Acyclic
Crown Ether Analogues.

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Smalley*, and (in part) Dalpat I. Patel,
The Ramage Laboratories, Department of Chemistry and
Applied Chemistry, University of Salford, Salford,
M5 4WT.

The mono-*o*-azidobenzoates (1a-c) of mono-, di-, and
tri-ethylene glycol on photolysis in methanol-tetra-
hydrofuran yield the corresponding glycol monoesters
(2a-c; R = H) of 2-methoxy- $3H$ -azepine-3-carboxylic acid.
A bis- $3H$ -azepine-3-carboxylate (4a) is obtained from
ethylene glycol di-*o*-azidobenzoate (3a). Similarly,
bis- $3H$ -azepine-3-carboxyamides (12, 13, and 14) are
obtained by ring-expansion of the di-*o*-azidobenzoyl
derivatives of ethylene, and *o*- and *p*-phenylene,
diamines.

Photolysis of the *o*-azidobenzoates of 2-ethoxyethanol
(6a) and diethylene glycol monomethyl ether (6b) in

mono- or di-ethylene glycol, or their monoalkyl ethers, and tetrahydrofuran produces 2-alkoxy-3H-azepine-3-carboxylates (5a, 5b, 7, and 8) one of which (8) has metal cation complexing properties.

Irradiation of β -hydroxyethyl α -azidobenzoate (1a) in tetrahydrofuran furnishes a diazepino 14-crown-4 analogue (18), whereas on spray pyrolysis indazolo [2,1-a]indazole-6,12-dione (24) is obtained. Mechanisms to explain the formation of these two unexpected products are proposed.

The thermal and photolytic induced ring-expansions of aryl azides to 2-substituted 3H-azepines in the presence of amines is well-documented.² However, ring-expansion in other nucleophilic solvents is less common, and with alcohols is effective only with an electron-withdrawing group in the aromatic nucleus, preferably at the ortho position to the azide function.^{3,4} These reactions have been exploited³⁻⁶ for the preparation of 2-alkoxy-3H-azepines bearing a variety of electron-withdrawing groups (e.g. CO₂R, CN, CF₃, CONHAr, and SO₂NHAr) in practicable yields. An extension of this simple and efficient process is now reported which allows the preparation of novel bis-3H-azepine-3-carboxylates (4) and -3-carboxyamides (12-14), and some dipodands⁷ (7 and 8) based on 2-alkoxy-3H-azepine-3-carboxylates.

α -Azidobenzoylation of mono-, di, and tri-ethylene

glycol in pyridine solution produced a mixture of the mono- and di-*o*-azidobenzoates (1a-c) and (3a-c) respectively, which were readily separated from each other by column chromatography. However, in the majority of cases an analytically pure sample could not be obtained as separation from high boiling glycol impurities was hampered by the instability (heat and light) of the azido-esters. The esters were, however, characterised satisfactorily by spectral data (i.r., mass, and p.m.r), and on photolysis in a 1:1 mixture of methanol-tetrahydrofuran ring-expanded to give the 2-methoxy-3H-azepine-3-carboxylates (2a-c; R = H). The yield of azepine decreased noticeably with increasing chain length of the glycol, and again the products proved to be difficult to separate from unidentified aliphatic by-products.

Diagram →
(1) - (4)

Of greater interest was the photolysis, under similar conditions, of the ethylene glycol di-*o*-azidobenzoate (3a), which furnished the bis-azepine-3-carboxylate (4a) in moderate yield (25%). Unfortunately, attempts to extend this novel double ring-expansion process to the corresponding di- and tri-ethylene glycol derivatives (3b, c) failed. Photolyses in methanol-tetrahydrofuran gave only resinous products. An alternative route to the bis-azepine (4b) involving photolysis of the *o*-azidobenzoyl derivative (2b; R = *o*-N₃C₆H₄CO) was also unsuccessful.

We were disappointed at these failures since the bis-azepine carboxylates (4), particularly that derived from triethylene glycol i.e. (4c), have structural features of open-chain crown ethers (podands⁷) and as such may well show metal cation complexing properties.

In an attempt to produce this type of structure an alternative approach was adopted in which the glycol moiety was introduced into the ester and the 2-alkoxy function of the 3H-azepine-3-carboxylate. It has been demonstrated¹ that methyl *o*-azidobenzoate undergoes ring-expansion to 2-alkoxy-3H-azepine-3-carboxylates in a variety of alcohols. In ethoxyethanol, and in diethylene glycol, -tetrahydrofuran solution, the azido-ester ring expands in a like manner to give the azepines (5a and 5b) respectively, in 60-70% yield.

→ Accordingly, the ethoxyethanol and the monomethyl ethylene glycol *o*-azidobenzoates (6a and 6b) were photolysed in their respective alcohols with tetrahydrofuran as co-solvent, to give the dipodands (7) and (8) respectively (50-55%) in which the 3H-azepine ring serves as the anchoring group.

The cation complexing abilities of azepines (7) and (8) were compared qualitatively with 15-crown-5 in the recently described⁸ 'dissolution in toluene' and 'the 1,3,5-trinitrobenzene-Meisenheimer complex colour' tests. Ester (7) gave negative results with a range of cations in both tests whereas with the

monomethyl ethylene glycol derivative (8) encouraging positive reactions were noted, particularly with lithium and potassium, and to a lesser extent, with barium and calcium, cations. Further studies in this area are continuing and will be reported elsewhere.

The success of the double ring-expansion of the bis-azidobenzoate (3a) to the bis-3H-azepine-3-carboxylate (4a) prompted a study of the photo-induced ring-expansion of bis-*o*-azidobenzoyl derivatives of other suitable bifunctional compounds. Initial results were discouraging in that the mono- and di- *o*-azidobenzoyl derivatives of ethanolamine (9a and 9b), *o*- (10a and 10e) and *p*-aminophenol (11b), catechol (10b and 10 c), quinol (11a and 11c), and *o*-aminothiophenol (10f) gave mainly tarry products along with small amounts of the corresponding triplet-nitrene derived amino-esters or amides. Previously³, difficulties have been encountered in preparing 3H-azepines in the presence of acidic groups e.g. phenols.

agrum
3) - (11)

→ In contrast, the bis-azepines (12), (13), and (14) were obtained in reasonable yields (20-43%) by photolysing the ethylene diamine, and the *o*- and *p*-phenylene diamine derivatives (9c), (10d), and (11d) respectively in methanol-tetrahydrofuran solution.

agrum
3) - (14)

→ The formation of 2-substituted-3H-azepines by photolysis or thermolysis of aryl azides in the presence of

nucleophiles is considered to involve nucleophilic attack at the reactive imine bond of either a benzazirine (15) or azacycloheptatetraene (16) intermediate[†] (Scheme 1). As far as we are aware intramolecular trapping of this intermediate by a suitably placed nucleophile has not been reported. Hence, decompositions of the ethylene glycol derivative (1a) were carried out in the hope that nucleophilic attack by the pendant hydroxyl group would trap the intermediate (15 or 16) to yield, ultimately, the fused 7:7 heterocyclic system (17).

Scheme 1 →

Thermolysis of the ester (1a) in *o*-dichlorobenzene (b.p. 178°C), in keeping with the behaviour of more simple alkyl *o*-azidobenzoates⁹, gave only tarry material and trace amounts of amino-ester. However, when photolysed in tetrahydrofuran in the absence of other nucleophiles, the ester yielded, in addition to much tar, a small amount (~10%) of a crystalline product the mass spectrum of which indicated a molecular weight of 358 i.e. twice that expected for the bicycle (17). A structure consistent with the spectral and analytical data is the diazepinotetraoxa-dioxocyclotetradecane (18). In the mass spectrum a double α -fission of the ester functions accounts for the base peak at m/z 179 units,

[†]Although spectroscopic evidence for both species is available¹⁰, the actual nature of the intermediate involved in ring expansions in solution, particularly of monocyclic aryl azides, is not yet clear.

whereas additional fragments at m/z 135 (15.2%) and 107 (14.9%) are consistent with further losses of OCH_2CH_2 (44 units) and CO (28 units), respectively. Also noteworthy is the secondary splitting of the triplet ethano proton resonances and of the upfield doublet (δ 2.9) characteristic of the azepine 3-proton.

Formation of this novel 14-crown-4 analogue was unexpected but presumably arises by intermolecular nucleophilic additions of the glycol side chain to an imine intermediate as exemplified in Scheme 2.

→ Lithium cations are known¹¹ to act as templates for 12-crown-4 ether formation. However, attempts to improve the yield of (18) by irradiating the glycol ester in tetrahydrofuran in the presence of lithium thiocyanate failed. Equally disappointing were the photolyses in tetrahydrofuran of the di- and tri- ethylene glycol esters (1b) and (1c); only resinous products were obtained.

Flash vacuum pyrolysis techniques have been used with great success for producing and trapping unusual, and in many instances, unstable thermolysis products from a wide range of systems.¹² Therefore, in a further attempt to trap intramolecularly, the intermediate (15) or (16), the glycol ester (1a) was subjected to Spray Vacuum Pyrolysis, a technique which has been developed recently¹³ for the pyrolysis of liquid and low melting samples. Pyrolysis of the ester at 320°C was messy and gave, along with much charred and resinous material, not

bicycle (17) but in low yield indazolo[2,1-a]indazole-6,12-dione (24) as the sole identifiable product.

Coincidentally, we have recently prepared this little known system by an alternative route¹⁴, and propose that its formation in the pyrolysis reaction occurs via the complex but preceded series of reactions outlined in Scheme 3.

Scheme 3 → Initial nitrene attack at the ester oxygen yields an ylide-like intermediate (19), which in the case of benzyl esters, rearranges to the isolable N-benzyl-2,1-benzisoxazolinone.¹⁵ However, production of reactive heterodienes of type (20) from 2,1-benzisoxazoles is well-documented¹⁶, as is their dimerisation (20→21) to 3,1-benzoxazin-4-ones by (4+2) cycloaddition of the iminoketen to the keten carbonyl group.¹⁷ Subsequent production of the nitrene (21→22) by elimination of the glycol side chains from the modified hydroxylamino groups is reasonable and parallels the generation of nitrenes by thermolysis of N,O-bis-trimethylsilyl hydroxylamines e.g. $\text{HN}(\text{SiMe}_3)\text{OSiMe}_3$.¹⁸ Finally, cyclisation of the nitrene (22) to the indazolo-benzoxazinone (23) and its subsequent rearrangement to the indazolo-indazolinone (24) has been described recently.¹⁴

Experimental

I.r. spectra were recorded as Nujol mulls or liquid films on a Perkin-Elmer 297 or 257 grating infrared spectrophotometer. ^1H and ^{13}C N.m.r. spectra were measured, unless otherwise stated, for CDCl_3 solutions (SiMe_4 as internal standard) on a Perkin-Elmer R 32 90 MHz and a Varian Associates CFT 20 spectrometer, respectively. Mass spectra were obtained on an A.E.I. MS 12 mass spectrometer, and u.v. spectra as ethanol solutions on a Unicam SP 800A spectrophotometer. The tetrahydrofuran (THF) used in the photolyses was dried (MgSO_4 and then sodium wire), and finally distilled under nitrogen from sodium and benzophenone. All m.p.s are uncorrected and distillation of all liquid samples was performed using a Kugelrohr. T.l.c. was on Alumina G (type E), whereas column chromatography was carried out on Alumina (type H).

o-Azidobenzoylations. - General method- o-Azido-
benzoylation of Ethylene Glycol. Freshly prepared³
o-azidobenzoyl chloride (14 g) was added dropwise over 15 min. to a cold stirred solution of ethylene glycol (4.8 g) in pyridine (30 ml.). The mixture was stirred at room temperature for 30 min. then poured into water (150 ml.) and extracted with diethyl ether (2x50 ml). The ether extracts were washed successively with hydrochloric acid (2x50 ml.) and water (2x50 ml.) and then dried over anhydrous MgSO_4 . Removal of the

ether left an oily mixture which was separated by column chromatography on alumina. Elution with a mixture of light petroleum (b.p. 80-100°C) and toluene (1:1) gave ethylene glycol bis-o-azidobenzoate (3a) (4.2g). Further elution with toluene yielded 2-hydroxyethyl o-azidobenzoate (8.3 g) as an oil which, by ^1H n.m.r. was shown to be contaminated with ethylene glycol. Repeated separation on alumina gave an analytically pure sample.

o-Azidobenzoylation of di- and tri- ethylene glycols were carried out in the same manner, as were the acylations of o-aminothiophenol, ethanolamine, o- and p- phenylene diamines, o- and p-aminophenol, and o- and p-hydroxyphenol. Analysis figures, yields, and other relevant data are given in Table 1. Spectroscopic data are listed in Table 2.

Photolysis of o-Azido- esters and amides in Alcohol-Tetrahydrofuran Solution. - General procedure. A stirred solution of the azido ester or amide (1.5-2.0 g) in a mixture of alcohol (150 ml) and dry tetrahydrofuran (150 ml) was photolysed (400 W medium pressure lamp with pyrex filter) in a ^awater-cooled photochemical reactor under nitrogen, until the azide [as shown by the disappearance of $\nu(\text{N}_3)$ at ca 2120 cm^{-1}] had decomposed (See Table 3 for irradiation times). The solvent was removed from the mixture under reduced pressure (rotary evaporator) and the oily or semi-solid residue chromatographed on alumina.

Products were purified further either by crystallisation or by distillation (bulb-to-bulb) under reduced pressure; see Table 3 for details.

Bis-*o*-azido -benzoates and -benzamides were treated in a similar manner. Physical data and analyses are given in Table 3, whereas n.m.r. spectroscopic data are contained in Tables 4 and 5.

Photolysis of *p*-Hydroxyethyl *o*-Azidobenzoate (1a) in Tetrahydrofuran. - A solution of *p*-hydroxyethyl *o*-azido-benzoate (2 g) in dry tetrahydrofuran (300 ml) was irradiated under the conditions outlined in the general method for 15 h. Evaporation of the solvent from the reaction mixture yielded an oily residue which was chromatographed on an alumina column. Elution with toluene-chloroform (9:1; v/v) gave bis-3H-azepino[2,3-b:2',3'-i]-1,5,8,12-tetraoxa-4,11-dioxo-cyclotetradecane (18) (0.2 g) as a white solid which crystallised from toluene m.p. 225°C. (Found: C, 60.2; H, 5.3; N, 7.75. $C_{18}H_{18}N_2O_6$ requires C, 60.3; H, 5.1; N, 7.8%); ν_{\max} (Nujol) 1740 (C=O) and 1620 (C=N) cm^{-1} ; δ_H (90 MHz, $CDCl_3$ -DMSO- d_6) 3.85-3.90 (2H, two overlapping doublets, 3- and 3'-H), 3.9-4.3 (4H, m, 2xCH₂), 4.55-4.95 (4H, m, 2xCH₂), 5.65-5.75 (2H, two overlapping doublets, 4- and 4'-H), 6.0-6.45 (4H, m, 5-, 5-, 6-, 5'-, and 6'-H), 7.0 (2H, d, 7- and 7'-H); δ_C (29.2 MHz, $CDCl_3$ -DMSO- d_6) 48.8 (d, C-3), 62.7 (t, CH₂), 65.0 (t, CH₂), 65.0 (t, CH₂), 115.3 (d, C-4), 116.2 (d, C-6), 125.9 (d, C-5), 136.6 (d, C-7), 144.7 (s, C-2), 168.0 (s, CO); m/z 358 (M⁺), 179 (M-179)⁺ (100%), 135 (15%), 107 (15%), 91 (18%), 80 (19%), and 79 (39.7%).

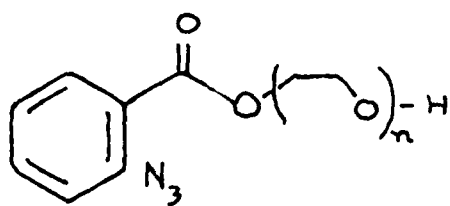
Spray Pyrolysis of β -(Hydroxyethyl) o-Azidobenzoate. -

β -Hydroxyethyl o-azidobenzoate (2.3 g) was subjected to Spray Vacuum Pyrolysis in the apparatus described.¹³ The azido-ester was admitted into the pyrolysis tube, which was packed with glass beads, and maintained at 320°C and 0.8 Torr, over a period of 2 h. After completion of pyrolysis, the pyrolysate, collected on the liquid nitrogen cooled cold-finger trap, was allowed to warm to room temperature and then washed, along with the pyrolysis tube, with dichloromethane. Evaporation of the washings gave a black tarry residue which was preabsorbed onto alumina and chromatographed (medium pressure column). Elution with light petroleum (b.p. 60-80°C)-ethyl acetate (7:3 v/v) gave indazolo[2,1-a]indazole-6,12-dione (24) (0.1 g; 5%), m.p. 298°C (identical in all respects to an authentic sample¹⁴) as the sole identifiable product. Further elution of the column with a variety of solvents gave only tarry fractions.

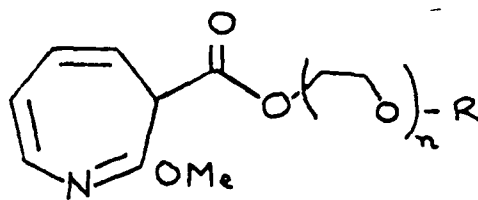
Complexation Tests of Dipodands (7) and (8) with Metal Cations. - These tests were carried out as directed in reference 8 and the results are given in Table 6.

Acknowledgements.

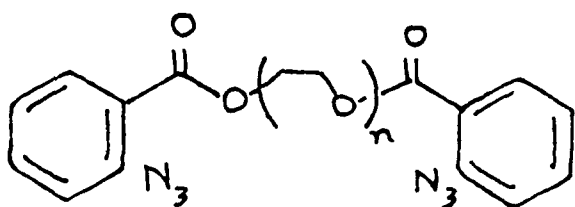
We thank the United States Army for support to (D. I. I.) through its European Research Office (Contract No. DAJA37-81-C-0763).



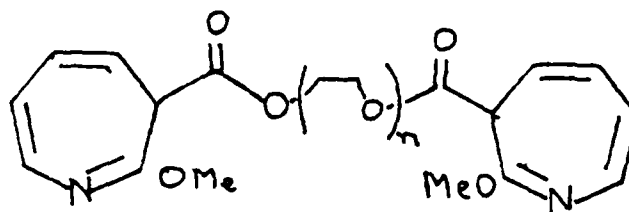
(1)



(2)

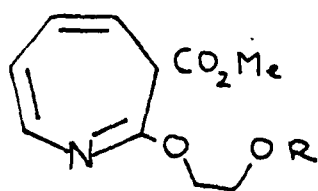
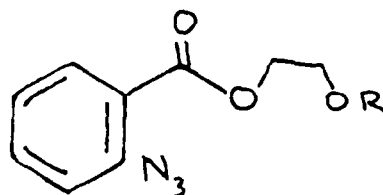


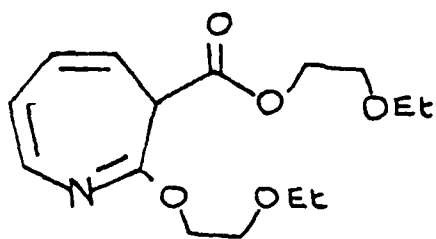
(3)



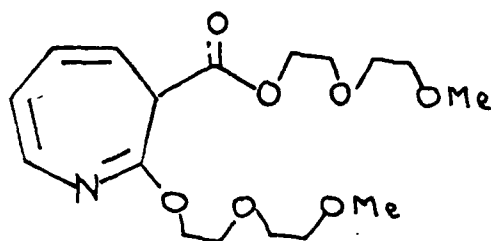
(4)

a, $n=1$; b, $n=2$; c, $n=3$

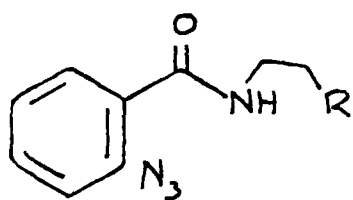
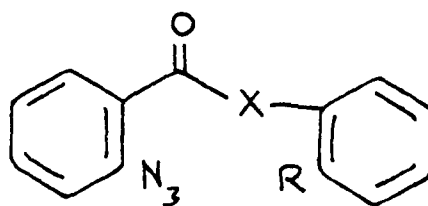
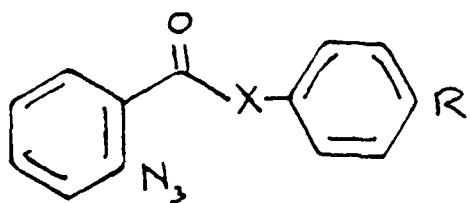
5 a $R = Et$ b $R = (CH_2)_2OH$ 6 a $R = Et$ b $R = (CH_2)_2OMe$

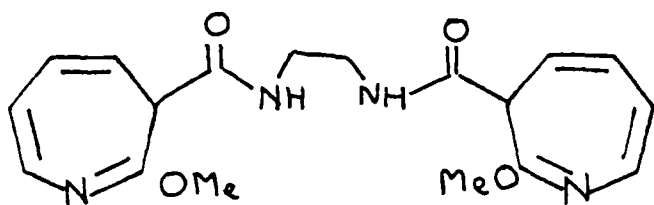


(7)

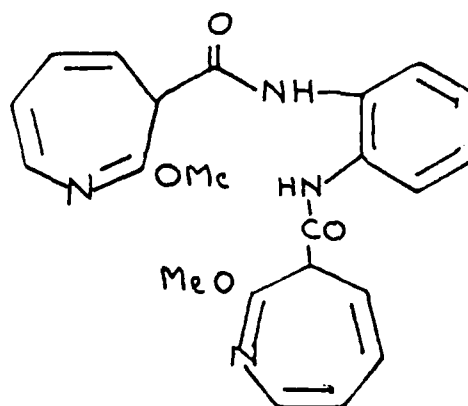


(8)

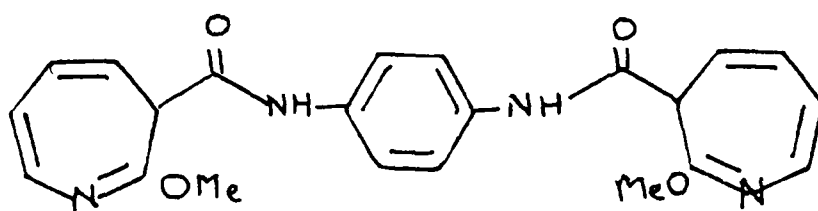
9 a $R = OH$ b $R = o-N_3C_6H_4CO_2-$ c $R = o-N_3C_6H_4CONH-$ 10 a $X = NH, R = OH$ b $X = O, R = OH$ c $X = O, R = o-N_3C_6H_4CO_2-$ d $X = NH, R = o-N_3C_6H_4CO_2-$ e $X = NH, R = o-N_3C_6H_4CO_2-$ f $X = S, R = o-N_3C_6H_4CONH-$ 11 a $X = O, R = OH$ b $X = NH, R = OH$ c $X = O, R = o-N_3C_6H_4CO_2-$



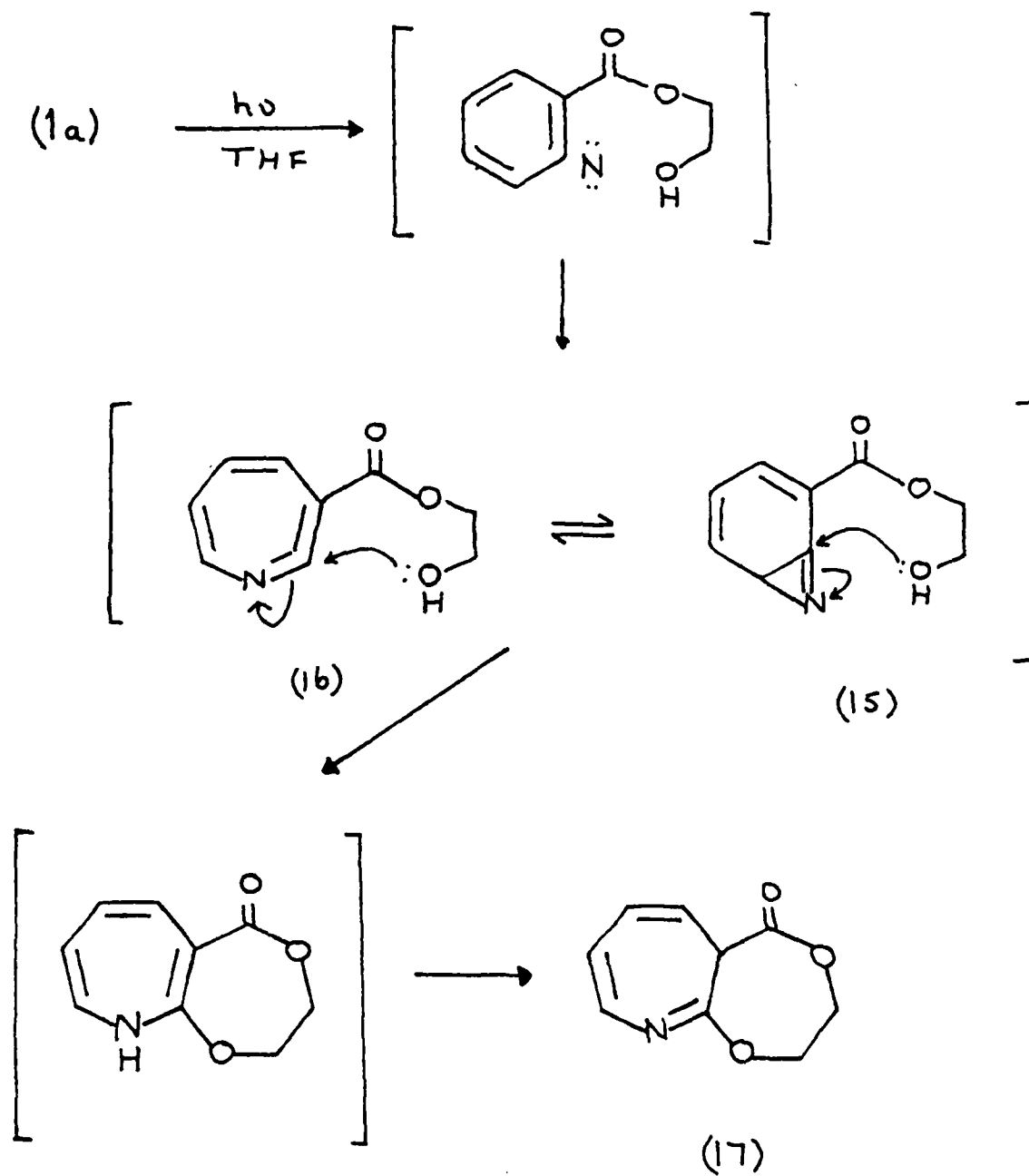
(12)



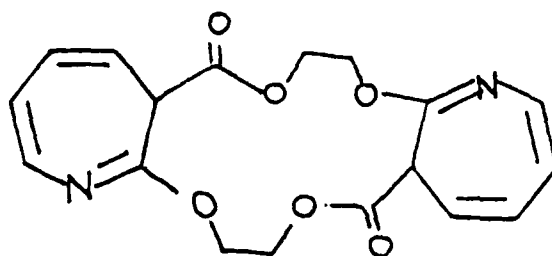
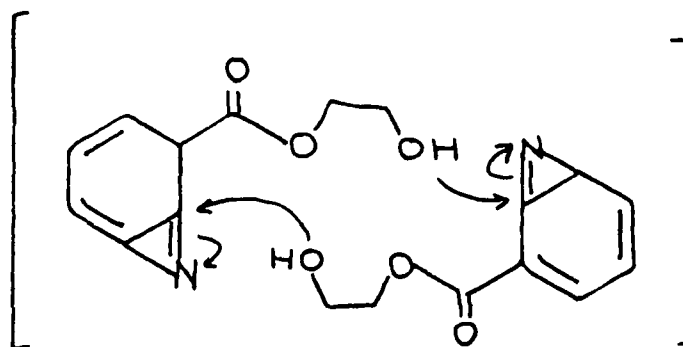
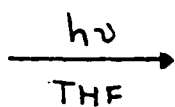
(13)



(14)

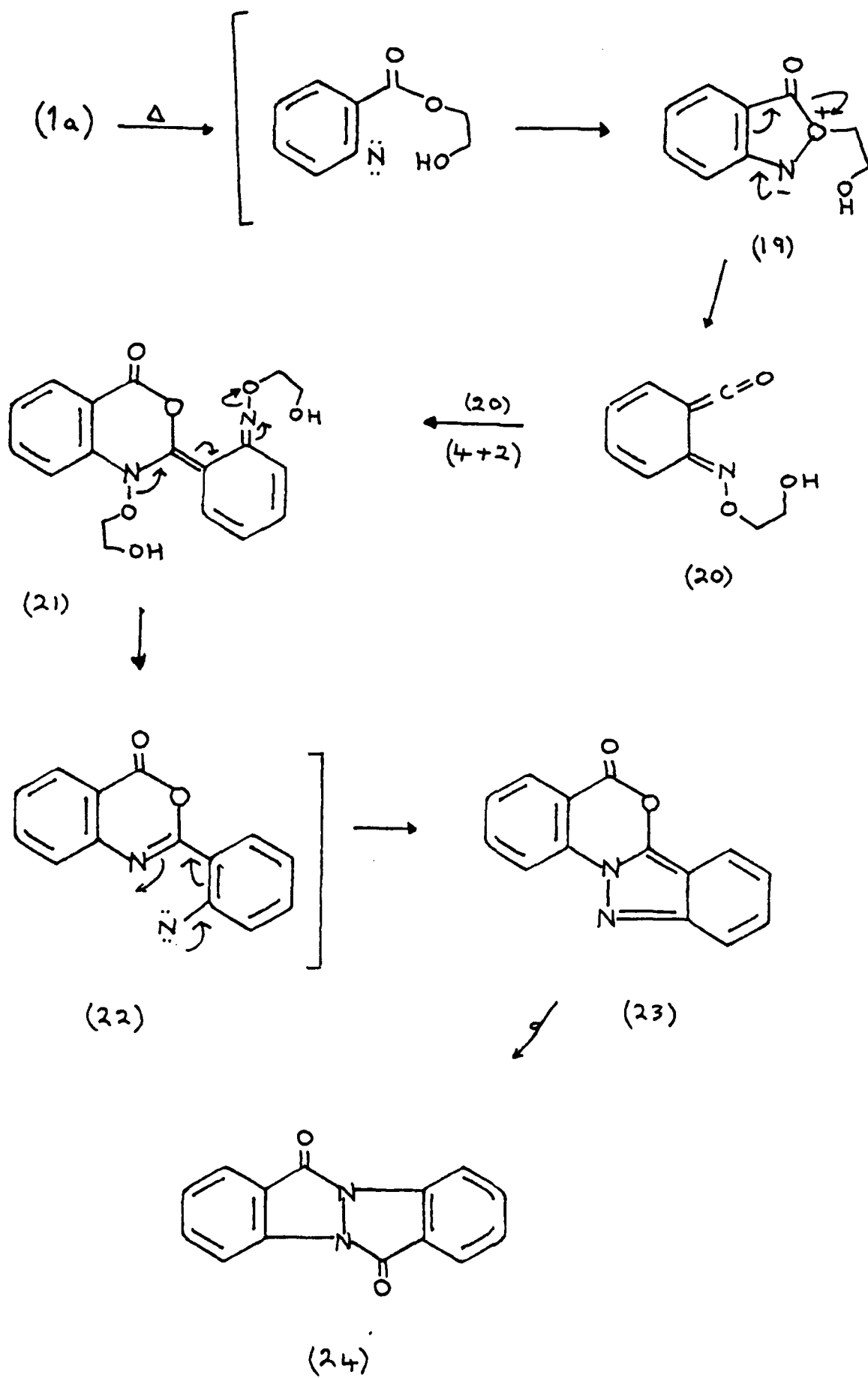
Scheme 1

(1a)



(18)

Scheme 2.



Scheme 10

Table 1. Mono- and di- o-azidobenzoyl derivatives

Compound No.	Yield (%)	m.p.(°C)	Found (%)			Mol. formula	Required (%)			m/z. M ⁺
		b.p.(°C)/ Torr.	C	H	N		C	H	N	
1a	54	- ^{a,e}	52.3	4.3	20.15	C ₉ H ₉ N ₃ O ₃	52.2	4.4	20.3	207
1b	46	- ^{a,d}								251
1c	52	- ^a								295
3a	32	74 ^{b,j}	54.8	3.4	23.8	C ₁₆ H ₁₂ N ₆ O ₄	54.5	3.4	23.8	352
3b	24	40 ^{b,j}	54.5	4.6	20.9	C ₁₈ H ₁₆ N ₆ O ₅	54.5	4.1	21.2	396
3c	24	- ^{a,g}								440
6a	58	- ^a								234
6b	53	- ^a								265
9a	61	67 ^b	52.4	4.8	27.0	C ₉ H ₁₀ N ₄ O ₂	52.4	4.85	27.1	206
9b	11	52 ^{b,i}	54.7	4.0	27.9	C ₁₆ H ₁₃ N ₇ O ₃	54.9	4.0	27.7	351
9c	91	188 ^e	54.8	4.2	32.1	C ₁₆ H ₁₄ N ₈ O ₂	54.8	4.0	32.0	
10a	83	161 ^f	61.2	3.9	22.3	C ₁₃ H ₁₀ N ₄ O ₂	61.4	4.0	22.0	
10b	60	95 ^{b,d}	61.2	3.5	16.6	C ₁₃ H ₉ N ₃ O ₃	61.2	3.3	16.5	
10c	12	111 ^{e,h}	60.2	2.9	20.8	C ₂₀ H ₁₂ N ₆ O ₄	60.0	3.0	21.0	
10d	35	164 ^{e,h}	60.2	3.6	28.2	C ₂₀ H ₁₄ N ₈ O ₂	60.3	3.3	28.1	
10e	79	129 ^{h,i}	59.9	3.3	24.5	C ₂₀ H ₁₃ N ₇ O ₃	60.1	3.3	24.6	
10f	20	148 ^{e,h,j}	57.8	3.3	23.5	C ₂₀ H ₁₃ N ₃ O ₂ S	57.8	3.1	23.6	
11a	80	146 ^{d,f}	61.4	3.6	16.1	C ₁₃ H ₉ N ₃ O ₃	61.2	3.5	16.5	
11b	85	188 ^{c,h}	61.4	3.8	22.4	C ₁₃ H ₁₀ N ₄ O ₂	61.4	4.0	22.0	
11c	10	122 ^{b,g}	60.1	3.2	20.1	C ₂₀ H ₁₂ N ₆ O ₄	60.0	3.0	21.0	
11d	50	205 ^k	60.0	3.2	28.1	C ₂₀ H ₁₄ N ₈ O ₂	60.3	3.5	28.1	

^a Oil; ^b Crystallised from light petroleum; ^c Eluted with CHCl₃-EtOH (95:5);

^d Eluted with PhMe-CHCl₃ (9:1); ^e Crystallised from HOCH₂CH₂OEt;

^f Crystallised from PhMe; ^g Eluted with PhMe; ^h Crystallised from ethanol;

ⁱ Prepared by o-azidobenzoylation of (10a); ^j bis-(o-aminodiphenyl) sulphide (40%);

obtained as by-product; ^k Crystallised from DMSO; ^l Prepared in excess of ethanolamine.

Table 2. Spectroscopic data for o-azido- esters and amides.

Compound	I.r. max:	¹ H n.m.r. (90 MHz; CDCl ₃)	
No.		Aromatics	Others.
1a	3450 (OH); 2120 (N ₃) 1720 (C=O)	7.1-8 (4H,m)	2.8 (1H,bs,OH), 3.9 (2H,t,CH ₂ OH), 4.4 (2H,t,COCH ₂)
1b	3450 (OH); 2130 (N ₃); 1730 (C=O)	7.1-8 (4H,m)	2.75 (1H,bs,OH) 3.75 (6H,m,3xCH ₂), 4.5 (2H,t,COCH ₂)
1c	3420 (OH); 2150 (N ₃) 1720 (C=O)	7.1-8 (4H,m)	2.7 (1H,bs,OH), 3.5- 3.9 (10H,m,5xCH ₂), 4.5 (2H,t,COCH ₂)
3a	2120 (N ₃); 1740 (C=O)	7.05-8 (8H,m)	4.5 (4H,s,2xCH ₂)
3b	2150 (N ₃); 1720 (C=O)	7.05-8 (8H,m)	3.9 (4H,t,-CH ₂ OCH ₂ -) 4.5 (4H,t,2xCO ₂ CH ₂)
3c	2140 (N ₃); 1720 (C=O)	7.05-8 (8H,m)	3.8 (8H,t,2x CH ₂ OCH ₂) 4.5 (4H,t,2xCO ₂ CH ₂)
6a	2120 (N ₃); 1720 (C=O)	7-8 (4H,m)	1.2 (3H,t,CH ₃), 3.6 (4H,m,-CH ₂ OCH ₂ -), 4.5 (2H,t,COCH ₂)
6b	2130 (N ₃); 1720 (C=O)	7-8 (4H,m)	3.4 (3H,s,OCH ₃), 3.65 (6H,m, -CH ₂ O(CH ₂) ₂ O-), 4.6 (2H,t,CO ₂ CH ₂)
9a	3400-3200 (NH) and (OH) 2125 (N ₃); 1680 (C=O)	7-8.2 (4H,m)	3.6-3.9 (4H,m,2xCH ₂), 4.25 (1H,bs,OH)
9b	3350 (NH), 2120 (N ₃), 1680 (C=O)	7.2-8.3 (8H,m)	4.6 (2H,t, -CH ₂ O), 3.8 (2H,t,CH ₂ N)
9c	3350 (NH), 2125 (N ₃), 1675 (C=O)	7.2-8.3 (8H,m)	3.9 (4H,s,2xCH ₂)

Table 3. Mono- and bis- 2-alkoxy-3H-azepine-3-carboxylates and -3- carboxyamides

Compound No.	Yield ^a (%)	b.p. (°C)/Torr (m.p. °C)	Found (%)			Mol. formula	Required (%)			m/z
			C	H	N		C	H	N	M ⁺
2a	56 ^{a,b}	120/0.2	57.1	6.1	6.8	C ₁₀ H ₁₃ NO ₄	56.9	6.2	6.6	211
2b	30 ^{a,c}	163/0.2	56.7	6.8	5.7	C ₁₂ H ₁₇ NO ₄	56.5	6.7	5.5	255
2c	30 ^{a,d}	179/0.2	56.7	7.1	4.7	C ₁₄ H ₂₁ NO ₆	56.2	7.1	4.7	299
4a	39 ^{d,e}	232/0.1	60.3	5.7	7.9	C ₁₈ H ₂₀ N ₂ O ₆	60.0	5.5	7.8	360
5a	70 ^{c,f}	130/0.4	60.7	7.3	6.3	C ₁₂ H ₁₇ NO ₄	60.2	7.2	5.9	239
5b	60 ^{c,f}	150/0.4	56.5	6.9	5.5	C ₁₂ H ₁₇ NO ₅	56.4	6.7	5.5	255
7	56 ^{d,g}	140/0.4	60.6	7.7	5.2	C ₁₅ H ₂₃ NO ₅	60.6	7.8	4.7	297
8	50 ^{f,h}	170/0.4	57.4	7.9	3.7	C ₁₇ H ₂₇ NO ₇	57.1	7.6	3.9	357
12	43 ^{d,i}	(209) ^j	60.3	6.0	15.7	C ₁₈ H ₂₂ N ₄ O ₄	60.3	6.2	15.6	358
13	39 ^{c,i,k}	(85) ^l	64.8	5.3	14.1	C ₂₂ H ₂₂ N ₄ O ₄	65.0	5.5	13.8	406
14	20 ^{c,k,m}	(246) ⁿ	65.0	5.4	13.6	C ₂₂ H ₂₂ N ₄ O ₄	65.0	5.5	13.8	406

* Yields are not optimised and figures cited refer to pure chromatographed and distilled (Kugelrohr), or crystallised, product.

^a Eluted with PhMe-CHCl₃ (9:1); ^b Irradiation time 4 h.; ^c Irradiation time 8 h.;

^d Irradiation time 10 h.; ^e Eluted with PhMe; ^f Eluted with light petroleum-EtOAc (9:1);

^g Eluted with light petroleum-EtOAc (1:1); ^h Irradiation time 12 h. ⁱ Eluted with CHCl₃;

^j Crystallised from EtOH; ^k Small amount of amino-ester also obtained ^l Crystallised from light petroleum-PhMe; ^m Eluted with CHCl₃-EtOH (9:1); ⁿ Crystallised from light petroleum (b.p. 100-120°C).

Table 4. ^1H n.m.r. data for mono- and bis- 2-alkoxy-
3H-azepine-3-carboxylates and -3-carboxyamides

Compound	Azepine ring(s)					2-Substituent	Others
	3-H	4-H	5-H	6-H	7-H		
2a	3.1 (d)	5.65 (dd)	6.27 (m)	6.08 (dd)	7.0 (d)	3.75 (3H, s, OMe)	4.3 (2H, t, CC_2CH_2), 3.8 (2H, t, CH_2OH), 3.0 (1H, bs, OH) x
2b	3.13 (d)	5.67 (dd)	6.26 (m)	6.05 (dd)	7.0 (d)	3.73 (3H, s, OMe)	4.4 (2H, t, CO_2CH_2 -), 3.7 (6H, m, $3\times\text{CH}_2$), 2.85 (1H bs, OH)
2c	3.13 (d)	5.67 (dd)	6.3 (m)	6.07 (dd)	7.0 (d)	3.75 (3H, s, OMe)	4.4 (2H, t, CO_2CH_2 -), 3.7 (10H, m, $5\times\text{CH}_2$), 2.7 (1H, bs, OH)
4a	3.1 (d)	5.67 (dd)	6.32 (dd)	6.08 (dd)	7.0 (d)	3.75 (6H, s, $2\times\text{OMe}$)	4.47 (4H s, $2\times\text{CH}_2$)
5a	3.1	5.7	6.4	6.2	7.0	1.1 (3H, t, CH_2CH_3), 3.6 (4H, m, $-\text{CH}_2\text{OCH}_2-$), 4.3 (2H, t, CH_2)	3.8 (3H, s, CC_2Me)
5b	3.1 (d)	5.7 (dd)	6.4 (m)	6.2 (dd)	6.9 (d)	2.8 (1H, b, OH), 3.6 (6H, m, $3\times\text{CH}_2$) 4.3 (2H, m, OCH_2)	3.8 (3H, s, CO_2Me)
7	3.2 (d)	5.7 (dd)	6.4 (m)	6.1 (dd)	7.0 (d)	a	a
8	3.1 (d)	5.5 - 6.5 (m)		7.0 (d)		b	b
12	3.32 (d)	5.63 (dd)	6.4 (dd)	6.0 (dd)	6.95 (d)	3.71 (6H, s, $2\times\text{OMe}$)	3.35 (4H s, $2\times\text{CH}_2$), 6.4 (2H, b, $2\times\text{NH}$)
13	3.4 (d)	5.65 (dd)	6.39 (dd)	6.0 (dd)	6.93 (d)	3.69 (3H, s, OMe) 3.62 (3H, s, OMe)	7-7.6 (4 H, m, ArH), 8.4 (2H, b, $2\times\text{NH}$)
14	2.95 (d)	5.77 (dd)	6.32 (dd)	6.09 (dd)	7.0 (d)	3.68 (3H, s, OMe) 3.6 (3H, s, OMe)	7.5-7.8 (4H, m, ArH) 9.95 (2H, b, $2\times\text{NH}$)

^a 1.2 (6H, overlapping triplets, $2\times\text{CH}_2\text{CH}_3$), 3.6 (8H, m, $4\times\text{CH}_2$), 4.3 (4H, overlapping triplets, $2\times\text{CH}_2$);

^b 3.4 (6H, s, $2\times\text{CH}_3$), 3.6 (12H, m, $6\times\text{CH}_2$), 4.3 (4H, m, $2\times\text{CH}_2$).

Table 5. ^{13}C N.m.r. Spectroscopic Data for 2-alkoxy-
3H-azepine-3-carboxylates.

Compound	Azepine ring							Others
	2-C	3-C	4-C	5-C	6-C	7-C	C=O	
2a	146 (s)	49.2 (d)	114.8 (d)	126.2 (d)	116 (d)	136.3 (d)	168.3 (s)	66.3 and 60.05 ($2\times\text{CH}_2$), 55.0 (q, OCH_3)
2b	145.8 (s)	48.9 (d)	114.5 (d)	126 (d)	115.7 (d)	136.3 (d)	167.8 (s)	71.9, 68.2, 63.8, and 60.8 ($4\times\text{CH}_2$), 54.7 (q, OCH_3)
2c	146.2 (s)	49.4 (d)	115 (d)	126.4 (d)	116 (d)	136.7 (d)	168.4 (s)	70.4, 70.2, 68.7, 64.2, 61.5, and 55.2 ($6\times\text{CH}_2$), 55.15 (q, OCH_3)
5b	145 (s)	49.2 (d)	114.4 (d)	126.05 (d)	116 (d)	136.3 (d)	168 (s)	67.4, 66.9, 65.8 ($3\times\text{CH}_2$), 51.4 (q, OCH_3), 14.5 (q, CH_3)
8	144.6 (s)	48.9 (d)	114.1 (d)	125.7 (d)	115.6 (d)	136.1 (d)	167.2 (s)	71.1, 69.6, 68.0, 66.5, and 63.5 ($8\times\text{CH}_2$), 57.85 (q, $2\times\text{OCH}_3$)

Table 6. Complexation Tests of Dipodands with Metal Cations.

Test Metal ion ^a Compound Test	Li ⁺		Na ⁺		NH ₄ ⁺		K ⁺		Ca ²⁺		Ba ²⁺	
	I ^d	II ^f	I ^b	II ^e	I ^d	II ^e	I ^h	II ^e	I ^c	II ^f	I ^d	II ^f
15-crown-5	+++ ^g	++	++	++	-	++	++	++	+	++	+++	++
7	-	-	-	-	-	-	-	-	-	-	-	-
8	+++	++	+	-	-	+	+++	++	+	-	++	-

^a Salts used were ^b bromide, ^c chloride, ^d iodide, ^e carbonate, and ^f hydroxide; ^g +++ represents an immediate positive test; ++ a positive test after 1 h.; and + a slow (>12h) positive test.

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Thermolysis of Aryl Azides in Phenyl Isocyanate

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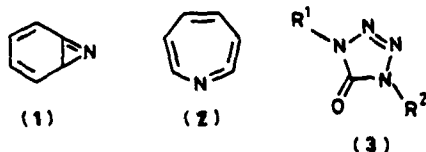
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Aryl azides ($p\text{-XC}_6\text{H}_4\text{N}_3$) decompose in boiling phenyl isocyanate to give mainly 1-phenyl-3-phenyl-carbamoyl-2-oxo-1,3-dihydrobenzimidazoles and azo-compounds. In some cases, however ($X = \text{Ac}$, CO_2Me , or CN) work-up in methanol solution produces methyl *N*-arylcarbamates ($p\text{-XC}_6\text{H}_4\text{NH}\cdot\text{CO}_2\text{Me}$) indicative of the formation of substituted isocyanates ($p\text{-XC}_6\text{H}_4\text{NCO}$) during thermolysis. A mechanistic rationale is offered.

The decomposition of aryl azides in nucleophilic solvents, e.g. amines is well-documented¹, and generally results in ring-expansion to 3*H*-azepines.

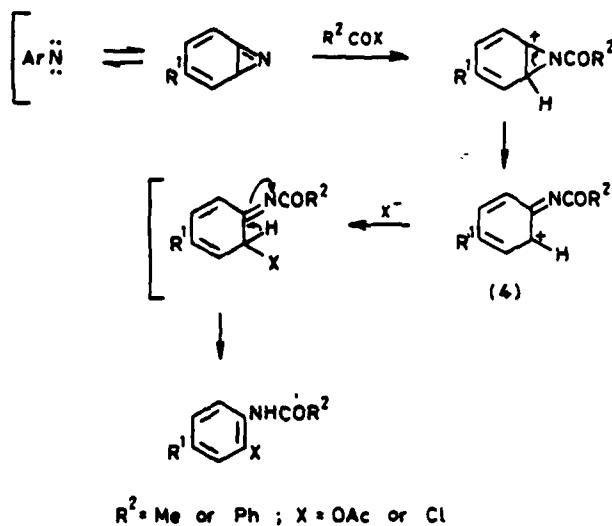
In contrast, we have found that with electrophilic reagents *ortho*-disubstituted benzenes are formed rather than azepines. For example, in hot acetic anhydride or benzoyl chloride, aryl azides decompose to yield *o*-aminophenols (initially as their *N,N,O*-triacyl derivatives)² and *o*-chlorobenzanilides,³ respectively.

The nature of the intermediate involved in nitrene-mediated ring-expansions and related reactions is currently the subject of debate, the two main contenders being the traditionally accepted benzazirine (1),⁴ and the more recently proposed and equally viable cumulated azacycloheptatetraene (2).^{5,6} Low-temperature ($< 10\text{ K}$) i.r. spectroscopic evidence in support of both species is available.⁷

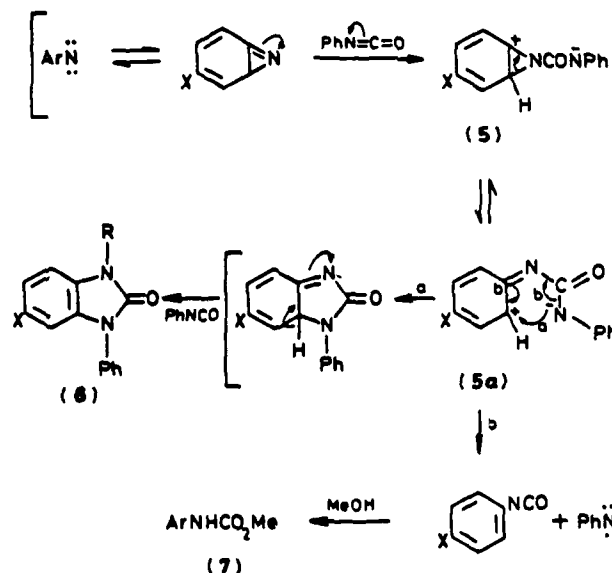


We have proposed a mechanistic rationale (Scheme 1) involving a benzazirine intermediate[†] to explain the formation of di- and tri-substituted arenes. On this basis we were hopeful that phenyl isocyanate would be sufficiently electrophilic to react with the benzazirine (or azacycloheptatetraene) and so yield, ultimately, 1-phenyl-2-oxo-1,3-dihydrobenzimidazoles (6) as outlined in Scheme 2.

Previous work on the decomposition of azides in isocyanates has been reported by L'Abbé,⁹ and by Lwowski,¹⁰ and their co-workers. The former found that at moderate temperatures (60°C) aryl azides fail to react with aryl isocyanates whereas alkyl azides undergo 1,3-dipolar cycloaddition with a variety of isocyanates (aryl, acyl, and sulphonyl) to yield tetrazolin-5-ones (3). In contrast, Lwowski found that photolysis or thermolysis of ethyl azidoformate in ethyl isocyanate produces the triazolinone (8; $\text{R}^1 = \text{CO}_2\text{Et}$, $\text{R}^2 = \text{Et}$). The high thermal stability (undecomposed at 250°C)⁹ precludes the triazolinone as a precursor of the triazolinone. In fact, the dione is thought to be formed by attack of the α -nitrogen of the azide at the isocyanate carbonyl followed by addition of a further molecule of isocyanate and cyclisation with loss of nitrogen as in Scheme 3.



Scheme 1.



Scheme 2.

[†] We acknowledge that an equally tenable reaction scheme can be drawn in which acylation of the azacycloheptatetraene is followed by ring-contraction of the resulting 1-acyl-1*H*-azepine.⁸

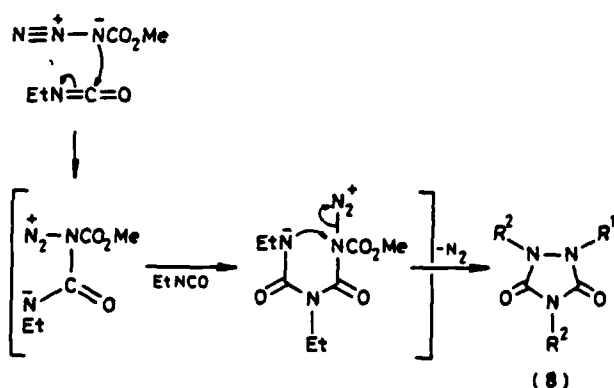
In view of these results we were surprised to find that aryl azides on thermolysis in boiling phenyl isocyanate yield, besides the ubiquitous azo-compounds, crystalline products of mole-

Table. Products from the decomposition of aryl azides in phenyl isocyanate.

	Azide $p\text{-XC}_6\text{H}_4\text{N}_3$	2-Oxo-1,3-dihydro- benzimidazole (6)	Azo-compound $(p\text{-XC}_6\text{H}_4\text{N})_2$	Other products† (% Yield)
	X	% Yield	% Yield	
a	H	14 (7.5)	12 (23)	—
b	OMe	27 (6.2)	8 (55)	—
c	Br	—	14.7	—
d	CN	—	26 (17.5)	$p\text{-NCC}_6\text{H}_4\text{NHCO}_2\text{Me}$ (36)
e	CH ₃	5.5	30	—
f	CO ₂ Me	9.3 (6.4)	22 (15)	$p\text{-MeO}_2\text{CC}_6\text{H}_4\text{NHCO}_2\text{Me}$ (10)
g	COMe	—	13	$p\text{-MeOCC}_6\text{H}_4\text{NHCO}_2\text{Me}$ (38)
h	CF ₃	5	18	—
i	NO ₂	—	—	Polymer

* Lower yields (figures in brackets) of 2-oxo-1,3-dihydrobenzimidazoles and variable yields of azobenzenes are obtained by heating a mixture of the two reactants under reflux rather than by adding the azide dropwise to boiling phenyl isocyanate.

† In all cases intractable tars are also obtained.

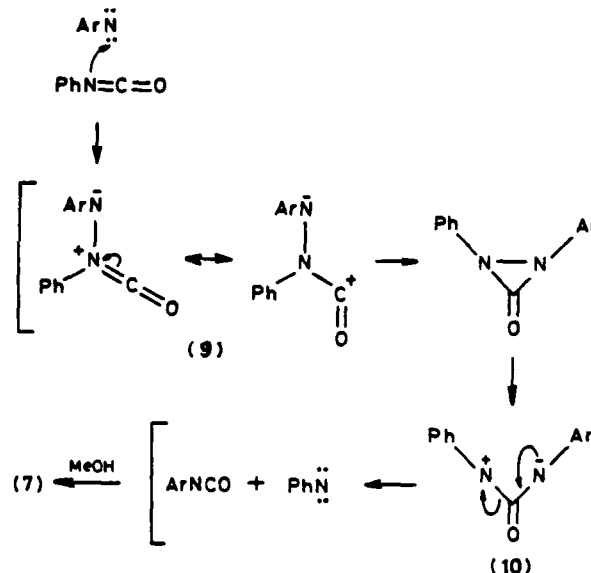


Scheme 3.

cular composition $\text{ArN} + 2\text{PhNCO}$ units. However, it soon became apparent that the product from the thermolysis of phenyl azide in phenyl isocyanate was not the triphenyl triazolinone (8; $\text{R}^1 = \text{R}^2 = \text{Ph}$), corresponding to the product obtained by Lwowski, but the known¹¹ 1-phenyl-3-phenylcarbamoyl-2-oxo-1,3-dihydrobenzimidazole (6; $\text{R} = \text{CONHPh}$, $\text{X} = \text{H}$). Mass, u.v., i.r., and ¹H n.m.r. data were in accord with literature values, and unequivocal proof of structure was obtained by comparison with an authentic sample prepared by heating 1-phenyl-2-oxo-1,3-dihydrobenzimidazole with phenyl isocyanate.

The results for the decomposition of substituted aryl azides in phenyl isocyanate are given in the Table. The structures of the benzimidazolinones were confirmed by elemental analysis and spectral data and in particular by their mass spectra which in every case showed loss of PhNCO ($M - 119$)⁺ as the base peak. A plausible explanation for the formation of the 1,3-disubstituted 2-oxobenzimidazoles is via carbamoylation of the benzimidazolinone formed initially, as predicted in Scheme 2 (path a).

In previous work on the thermolysis of aryl azides in acylating agents^{2,3} significant increases in product yields were noted with electron donating *para*-substituents (e.g. $\text{R}^1 = \text{MeO}$ or Me ; Scheme 1). It was argued³ that such substituents stabilise, by mesomeric interactions, the positively charged intermediate (4) and hence promote regioselective ring-opening



Scheme 4.

of the aziridine ring to yield products in which the nitrogen function retains its position relative to the substituent (R^1), i.e. no 'nitrogen walk'.¹² In a similar manner we expected the yield of benzimidazolinone (6) to be influenced by substituent X. However, no obvious trend in substituent effect is apparent from the results given in the Table. Curiously, however, there is a marked difference in behaviour of some azides bearing electron-withdrawing groups. For example, the isolation of carbamates (7) from the thermolyses of *p*-cyano-, *p*-acetyl-, and *p*-methoxycarbonyl-phenyl azides in phenyl isocyanate is intriguing and can only be explained by the generation, during the thermolysis, of the correspondingly substituted aryl isocyanate and its subsequent trapping by methanol during work-up.

A feasible, but as yet speculative mechanism to explain these anomalous products is that the polar intermediate ($5 = 5a$) is destabilised by the electron-withdrawing group X and so fragments to ArNCO and PhN (as in Scheme 2; path b) rather than ring-closing to the benzimidazolinone. Alternatively, it is

possible that with these more electrophilic nitrenes, attack by the nitrene takes place initially at the isocyanate* to yield the resonance-stabilised ylide-like intermediate (9), which by rearrangement to the alternative dipolar structure (10) can, by retro-addition, furnish the substituted isocyanate and phenyl nitrene (Scheme 4).

The structures of the carbamates (Table) have been confirmed by unambiguous synthesis and spectroscopic data.

Variations in the reaction conditions have given disappointing results. For example, a decomposition of phenyl or *p*-methoxyphenyl azide in a 10% solution of phenyl isocyanate in xylene produced, in addition to much tar, only the *N,N'*-diarylurea. Presumably, the nitrene, as the triplet species, is abstracting hydrogen from the solvent to give arylamines (a well-known process¹) which with isocyanate furnishes the urea.

Experimental

I.r. spectra were recorded as Nujol mulls or liquid films on a Perkin-Elmer 297 or 257 grating i.r. spectrophotometer. ¹H N.m.r. spectra were measured for CDCl₃ solutions (SiMe₄ as internal standard) on a Perkin-Elmer R-32 90 MHz spectrometer. Mass spectra were obtained on an A.E.I. MS12 mass spectrometer, and u.v. spectra as methanol solutions on a Unicam SP800A spectrophotometer. All m.p.s are uncorrected. T.l.c. was on Alumina G (type E) whereas column chromatography was carried out on Alumina (type H).

Preparation of Aryl Azides.—The aryl azides were prepared as reported previously¹³ from the arylamines, by diazotisation and subsequent azidation with sodium azide in buffered (sodium acetate) solution. They were purified by chromatography on alumina, with light petroleum (b.p. 40–60 °C) as eluant.

Thermolysis of Aryl Azides (p-XC₆H₄N₃) in Phenyl Isocyanate: General Method.—The aryl azide was added dropwise to a boiling solution of freshly distilled phenyl isocyanate. The mixture was heated under reflux until azide decomposition was complete, as shown either by disappearance of ν(N₃) at 2 120 cm⁻¹ or by t.l.c. The mixture was cooled and the excess of phenyl isocyanate removed either by vacuum distillation (water pump), or better by conversion into methyl *N*-phenylcarbamate by addition of methanol (50 ml). In the latter case, excess of methanol was removed by distillation (rotary evaporator) and the residual semisolid distilled carefully (bulb-to-bulb) to remove the *N*-phenyl carbamate. The final residue was separated by column chromatography.

Products, % yields, and reaction times are given in the Table. Chromatographic separations were achieved on alumina and unless stated otherwise azo-compounds were eluted first, with light petroleum (b.p. 60–80 °C) as eluant, followed successively by the 2-oxobenzimidazoles and the methyl *N*-arylcarbamates (7) [light petroleum (b.p. 60–80 °C)–ethyl acetate (1:1; v/v) as eluant].

(a) Phenyl azide (0.87 g) in phenyl isocyanate (10 ml) gave on chromatographic separation azobenzene (0.16 g), m.p. 68 °C, and 3-phenyl-1-phenylcarbamoyl-2-oxo-1,3-dihydrobenzimidazole (6a) (0.33 g), m.p. 172 °C (from light petroleum–ethyl acetate) (lit.¹¹ m.p. 168 °C) (Found: C, 73.0; H, 4.6; N, 12.7. Calc. for C₂₀H₁₃N₃O₂: C, 72.9; H, 4.6; N, 12.8%). *m/z* 329 (*M*⁺) and 210 (*M* – 119)⁺ (100%). ¹H N.m.r. and i.r. spectra were in agreement with published values.¹¹

(b) *p*-Methoxyphenyl azide (2 g) in phenyl isocyanate (20 ml) gave on chromatographic separation 4,4'-dimethoxyazobenzene (0.27 g), m.p. 162 °C (lit.¹⁴ m.p. 162 °C) and 6-methoxy-1-phenyl-3-phenylcarbamoyl-2-oxo-1,3-dihydrobenzimidazole (6b) (1.3 g), m.p. 181 °C (from light petroleum–ethyl acetate) (Found: C, 70.05; H, 4.7; N, 11.8. C₂₁H₁₇N₃O₃ requires C, 70.2; H, 4.8; N, 11.7%). *v*_{max} (Nujol) 3 200–3 000 (NH), 1 680, and 1 720 cm⁻¹ (C=O); *λ*_{max} (log ε) (MeOH) 230 (4.45) and 245.5 (4.39) nm; *δ*_H (90 MHz; CDCl₃) 3.75 (3 H, s, OMe), 6.55–7.80 (12 H, m, ArH), 8.3 (1 H, d, *J* 7 Hz, 4-H), and 10.9 (1 H, br, NH); *m/z* 359 (*M*⁺) and 240 (*M* – 119)⁺ (100%).

(c) *p*-Bromophenyl azide (1 g) in phenyl isocyanate (10 ml) on chromatographic separation gave 4,4'-dibromoazobenzene (0.25 g), m.p. 204 °C (lit.¹⁵ m.p. 205 °C) and tarry material.

(d) *p*-Cyanophenyl azide (0.5 g) in phenyl isocyanate (10 ml) on chromatographic separation gave 4,4'-dicyanoazobenzene (0.14 g), m.p. 272 °C (lit.¹⁶ m.p. 272 °C), and methyl *N*-(*p*-cyanophenyl)carbamate (7; Ar = *p*-NCC₆H₄) (0.22 g), m.p. 149 °C (Found: C, 61.1; H, 4.5; N, 15.8. C₉H₈N₂O₂ requires C, 61.4; H, 4.6; N, 15.9%). *v*_{max} (Nujol) 3 340 (NH), 2 220 (CN), and 1 700 (CO) cm⁻¹; *δ*_H (90 MHz; CDCl₃) 3.8 (3 H, s, OMe), 7.05 (1 H, br, NH), and 7.5 (4 H, br s, ArH); *m/z* 176 (*M*⁺).

The carbamate was identical with an authentic sample prepared by condensing *p*-cyanoaniline with methyl chloroformate in hot pyridine solution.

(e) *p*-Methylphenyl azide (0.9 g) in phenyl isocyanate (10 ml) on chromatographic separation gave 4,4'-dimethylazobenzene (0.45 g), m.p. 145 °C (lit.¹⁷ m.p. 114 °C) and 6-methyl-1-phenyl-3-phenylcarbamoyl-2-oxo-1,3-dihydrobenzimidazole (6e) (0.12 g), m.p. 163 °C (from light petroleum–ethyl acetate) (Found: C, 73.3; H, 4.9; N, 12.3. C₂₁H₁₇N₃O₂ requires C, 73.45; H, 5.1; N, 12.2%). *v*_{max} (Nujol) 3 000–3 200 (NH), 1 725, and 1 695 (CO) cm⁻¹; *λ*_{max} (MeOH) 214 (4.42) and 245 (4.44) nm; *δ*_H (90 MHz; CDCl₃) 2.5 (3 H, s, Me), 7.1–7.9 (12 H, m, ArH), 8.5 (1 H, d, *J* 7 Hz, 4-H), 10.95 (1 H, br, NH); *m/z* 343 (*M*⁺) and 224 (*M* – 119)⁺ (100%).

(f) Methyl *p*-azidobenzoate (1 g) in phenyl isocyanate (10 ml) gave, on cooling of the reaction mixture, 4,4'-bismethoxycarbonylazobenzene (0.36 g), m.p. 197 °C (lit.¹⁸ 198 °C). Chromatographic separation, light petroleum (b.p. 60–80 °C)–ethyl acetate (1:2 v/v), gave 6-methoxycarbonyl-1-phenyl-3-phenylcarbamoyl-2-oxo-1,3-dihydrobenzimidazole (6f) (0.22 g), m.p. 199 °C (from light petroleum–ethyl acetate) (Found: C, 68.2; H, 4.45; N, 10.7. C₂₂H₁₇N₃O₄ requires C, 68.0; H, 4.4; N, 10.85%). *v*_{max} (Nujol) 3 000–3 200 (NH), 1 705, and 1 725 (CO) cm⁻¹; *λ*_{max} (log ε) (MeOH), 211.5 and 239 (4.37); *δ*_H (90 MHz; CDCl₃) 3.85 (3 H, s, OMe), 7.05–8.1 (12 H, m, ArH), 8.35 (1 H, d, *J* 7 Hz, 4-H), and 10.95 (1 H, br, NH); *m/z* 387 (*M*⁺) and 268 (*M* – 119)⁺ (100%).

Further elution gave methyl *N*-(4-methoxycarbonylphenyl)carbamate (7; Ar = 4-MeO₂CC₆H₄) (0.12 g), m.p. 170 °C (Found: C, 57.5; H, 5.3; N, 6.7. C₁₀H₁₁NO₄ requires C, 57.4; H, 5.3; N, 6.7%). *v*_{max} (Nujol) 3 300 (NH), 1 725 and 1 695 (CO) cm⁻¹; *δ*_H (90 MHz; CDCl₃) 3.75 (3 H, s, OMe), 3.85 (3 H, s, OMe), 7.0 (1 H, br, NH), 7.45 (2 H, d, *J* 7 Hz, 3- and 5-H), and 8.0 (2 H, d, *J* 7 Hz, 2- and 6-H).

The product was identical with the *N*-arylcarbamate prepared by heating a mixture of methyl *p*-aminobenzoate (5 g) with methyl chloroformate (2.6 g) in pyridine (20 ml) for 2 h.

(g) *p*-Azidoacetophenone (1 g) in phenyl isocyanate (10 ml) on chromatographic separation gave 4,4'-diacetylazobenzene (0.22 g) m.p. 218 °C (Found: C, 71.95; H, 5.3; N, 10.5. C₁₆H₁₄N₂O₂ requires C, 72.2; H, 5.3; N, 10.9%). Further elution with a (4:1) mixture of light petroleum (b.p. 60–80 °C) and ethyl acetate gave methyl *N*-(4-acetylphenyl)carbamate (7; Ar = 4-AcC₆H₄), m.p. 164 °C (lit.¹⁹ m.p. 162 °C); *v*_{max} 3 310 (NH), 1 730 and 1 690 (C=O) cm⁻¹; *δ*_H (90 MHz; CDCl₃) 2.55 (3 H, s, COCH₃), 3.8 (3 H, s, CO₂CH₃), 7.35 (1 H, b, NH), 7.55

* It is most unlikely under our reaction conditions, that the α -nitrogen of the azide is the attacking species as suggested by Lwowski¹⁰ in related reactions (Scheme 3).

(2 H, d, 7.7 Hz, 2- and 5-H), and 8.0 (2 H, d, 7.7 Hz, 2- and 5-H). The product was identical with the *N*-arylcarbamate prepared by heating *p*-aminoacetophenone with methyl chloroformate in pyridine solution.

(h) *p*-(Trifluoromethyl)phenyl azide (1.5 g) in phenyl isocyanate (15 ml) on chromatographic separation gave 4,4'-bis(trifluoromethyl)azobenzene (0.31 g), m.p. 101 °C (lit.,¹⁶ m.p. 102 °C), followed by 1-phenyl-3-phenylcarbamoyl-6-trifluoromethyl-2-oxo-1,3-dihydrobenzimidazole (6h) (0.11 g), m.p. 196 °C (from light petroleum-ethyl acetate) (Found C, 63.5; H, 3.55; N, 10.6. C₂₁H₁₄F₃N₃O₂ requires C, 63.4; H, 3.5; N, 10.5%); ν_{\max} (Nujol) 3 200–3 000 (NH), 1 720 and 1 690 (CO) cm⁻¹; λ_{\max} (log ϵ) (MeOH) 212 (4.42), and 247 (4.33) nm; δ_{H} (90 MHz; CDCl₃) 7.3–8.4 (12 H, m, ArH), 8.85 (1 H, m, 4-H), 10.95 (1 H, s, NH); m/z 397 (M^+) and 278 ($M - 119$)⁺ (100%).

(i) 4-Nitrophenyl azide (0.5 g) in phenyl isocyanate (10 ml) gave a black polymeric material from which no identifiable products were isolated.

Acknowledgements

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